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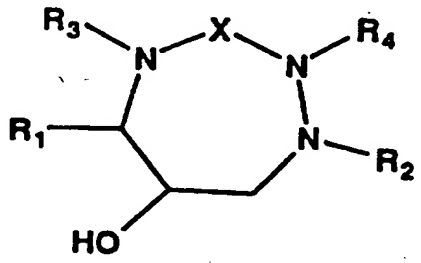
(54) Title: RETROVIRAL PROTEASE INHIBITING 1,2,4-TRIAZACYCLOHEPTANES



(A)

(57) Abstract

A retriviral protease inhibiting compound of formula (A) is disclosed.

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RETROVIRAL PROTEASE INHIBITING COMPOUNDS

This is a continuation-in-part of U.S. patent application Serial No. 286,380, filed August 9, 1994.

Technical Field

The present invention relates to novel compounds and a composition and method for inhibiting retroviral proteases and in particular for inhibiting human immunodeficiency virus (HIV) protease, a composition and method for treating a retroviral infection and in particular an HIV infection, processes for making such compounds and synthetic intermediates employed in these processes.

Background of the Invention

Retroviruses are those viruses which utilize a ribonucleic acid (RNA) intermediate and a RNA-dependent deoxyribonucleic acid (DNA) polymerase, reverse transcriptase, during their life cycle. Retroviruses include, but are not limited to, the RNA viruses of the Retroviridae family, and also the DNA viruses of the Hepadnavirus and Caulimovirus families. Retroviruses cause a variety of disease states in man, animals and plants. Some of the more important retroviruses from a pathological standpoint include human immunodeficiency

viruses (HIV-1 and HIV-2), which cause acquired immune deficiency syndrome (AIDS) in man, hepatitis B virus, which causes hepatitis and hepatic carcinomas in man, human T-cell lymphotrophic viruses I, II, IV and V, which cause human acute cell leukemia, and bovine and feline leukemia viruses which cause leukemia in domestic animals.

Proteases are enzymes which cleave proteins at specific peptide bonds. Many biological functions are controlled or mediated by proteases and their complementary protease inhibitors. For example, the protease renin cleaves the peptide angiotensinogen to produce the peptide angiotensin I. Angiotensin I is further cleaved by the protease angiotensin converting enzyme (ACE) to form the hypotensive peptide angiotensin II. Inhibitors of renin and ACE are known to reduce high blood pressure in vivo. An inhibitor of a retroviral protease will provide a therapeutic agent for diseases caused by the retrovirus.

The genomes of retroviruses encode a protease that is responsible for the proteolytic processing of one or more polyprotein precursors such as the pol and gag gene products. See Wellink, Arch. Virol. 98 1 (1988). Retroviral proteases most commonly process the gag precursor into core proteins, and also process the pol precursor into reverse transciptase and retroviral protease. In addition, retroviral proteases are sequence specific. See Pearl, Nature 328 482 (1987).

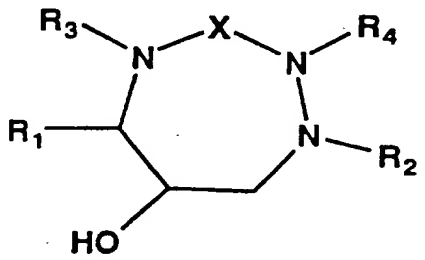
The correct processing of the precursor polyproteins by the retroviral protease is necessary for the assembly of infectious virions. It has been shown that in vitro mutagenesis that produces protease-defective virus leads to the production of immature core forms which lack infectivity. See Crawford, J. Virol. 53 899 (1985); Katoh, et al., Virology 145 280 (1985). Therefore, retroviral protease inhibition provides an attractive target for antiviral therapy. See Mitsuya, Nature 325 775 (1987).

Current treatments for viral diseases usually involve administration of compounds that inhibit viral DNA synthesis. Current treatments for AIDS involve administration of compounds such as 3'-azido-3'-deoxythymidine (AZT), 2',3'-dideoxycytidine (ddC), 2',3'-dideoxyinosine (ddI) and 2',3'-didehydro-3'-deoxythymidine (d4T) and compounds which treat the opportunistic infections caused by the immunosuppression resulting from HIV infection. None of the current AIDS treatments have proven to be totally effective in treating and/or

reversing the disease. In addition, many of the compounds currently used to treat AIDS cause adverse side effects including low platelet count, renal toxicity and bone marrow cytopenia.

Disclosure of the Invention

In accordance with the present invention, there are compounds of the formula **A**:



A

wherein R_1 is selected from:

(i) hydrogen,
(ii) loweralkyl,
(iii) aryl,
(iv) thioalkoxyalkyl,
(v) (aryl)alkyl,
(vi) cycloalkyl,
(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,
(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,
(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,

(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,
(xx) loweralkenyl,
(xxi) heterocyclic,
(xxii) (heterocyclic)alkyl),
(xxiii) arylthioalkyl,
(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,
(xxvii) (heterocyclic)oxyalkyl,
(xxviii) arylalkoxyalkyl,
(xxix) arylthioalkoxyalkyl,
(xxx) arylalkylsulfonylalkyl,
(xxxi) (heterocyclic)alkoxyalkyl,
(xxxii) (heterocyclic)thioalkoxyalkyl,
(xxxiii) (heterocyclic)alkylsulfonylalkyl,
(xxxiv) cycloalkyloxyalkyl,
(xxxv) cycloalkylthioalkyl,
(xxxvi) cycloalkylsulfonylalkyl,
(xxxvii) cycloalkylalkoxyalkyl,
(xxxviii) cycloalkylthioalkoxyalkyl,
(xxxix) cycloalkylalkylsulfonylalkyl,
(xl) aminocarbonyl,
(xli) alkylaminocarbonyl,
(xlii) dialkylaminocarbonyl,
(xliii) aroylalkyl,
(xliv) (heterocyclic)carbonylalkyl,
(xlv) polyhydroxyalkyl,
(xlvi) aminocarbonylalkyl,
(xlvii) alkylaminocarbonylalkyl,
(xlviii) dialkylaminocarbonylalkyl,
(xlix) aryloxyalkyl,
(l) alkylsulfonylalkyl and
(li) arylalkoxycarbonylalkyl;

R_2 is R_{2a}-C(O)- or R_{2a}-S(O)$_2$- wherein R_{2a} is selected from:

(i) loweralkyl,
(ii) loweralkenyl,
(iii) cycloalkyl,
(iv) cycloalkenyl,
(v) cycloalkylalkyl,
(vi) cycloalkenylalkyl,
(vii) hydroxyalkyl,
(viii) alkoxyalkyl,
(ix) aminoalkyl,
(x) alkylaminoalkyl,
(xi) dialkylaminoalkyl,
(xii) aryl,
(xiii) arylalkyl,
(xiv) heterocyclic,
(xv) (heterocyclic)alkyl and
(xvi) alkoxy;

R_3 and R_4 are independently selected from:

(i) hydrogen,
(ii) loweralkyl,
(iii) aryl,
(iv) thioalkoxyalkyl,
(v) (aryl)alkyl,
(vi) cycloalkyl,
(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,

(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,
(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,
(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,
(xx) loweralkenyl,
(xxi) heterocyclic,
(xxii) (heterocyclic)alkyl),
(xxiii) arylthioalkyl,
(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,
(xxvii) (heterocyclic)oxyalkyl,
(xxviii) arylalkoxyalkyl,
(xxix) arylthioalkoxyalkyl,
(xxx) arylalkylsulfonylalkyl,
(xxxi) (heterocyclic)alkoxyalkyl,
(xxxii) (heterocyclic)thioalkoxyalkyl,
(xxxiii) (heterocyclic)alkylsulfonylalkyl,
(xxxiv) cycloalkyloxyalkyl,
(xxxv) cycloalkylthioalkyl,
(xxxvi) cycloalkylsulfonylalkyl,
(xxxvii) cycloalkylalkoxyalkyl,
(xxxviii) cycloalkylthioalkoxyalkyl,
(xxxix) cycloalkylalkylsulfonylalkyl,
(xl) aroylalkyl,
(xli) (heterocyclic)carbonylalkyl,
(xlii) polyhydroxyalkyl,
(xliii) aminocarbonylalkyl,
(xliv) alkylaminocarbonylalkyl,
(xlv) dialkylaminocarbonylalkyl,
(xlv) aryloxyalkyl,
(xlvi) alkylsulfonylalkyl,

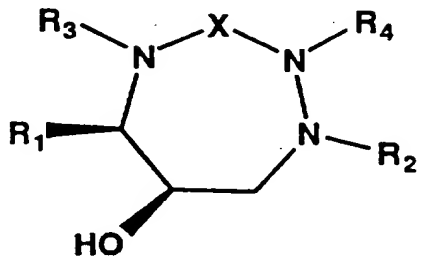
(xlvii) carboxyalkoxyalkyl,
(xlviii) (alkoxycarbonyl)alkoxyalkyl,
(xlix) (amino)carboxyalkyl,
(l) ((N-protected)amino)carboxyalkyl,
(li) (alkylamino)carboxyalkyl,
(lii) ((N-protected)alkylamino)carboxyalkyl,
(liii) (dialkylamino)carboxyalkyl,
(liv) (amino)alkoxycarbonylalkyl,
(lv) ((N-protected)amino)alkoxycarbonylalkyl,
(lvi) (alkylamino)alkoxycarbonylalkyl,
(lvii) ((N-protected)alkylamino)alkoxycarbonylalkyl,
(lviii) (dialkylamino)alkoxycarbonylalkyl,
(lix) (polyalkoxy)alkyl,
(lx) (hydroxyamino)alkyl,
(lxi) (alkoxyamino)alkyl,
(lxii) dihydroxyalkyl,
(lxiii) (alkoxy)(alkyl)aminoalkyl and
(lxiv) arylalkoxycarbonylalkyl; and

X is

(i) -C(=Y)- wherein Y is O, S or N(R_5) wherein R_5 is loweralkyl, hydroxy, amino, alkylamino, dialkylamino, alkoxy, benzyloxy, cyano or nitro;
(ii) -S(O)- or
(iii) -$S(O)_2$-;

or a pharmaceutically acceptable salt, ester or prodrug thereof.

Preferred compounds of the invention are compounds of the formula B:



B

wherein R_1, R_2, R_3, R_4 and X are defined as above.

Preferred compounds of the invention are compounds of the formula **A** or **B** wherein R_1 is loweralkyl or arylalkyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is loweralkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, aryl or arylalkyl; R_3 and R_4 are independently selected from loweralkyl, loweralkenyl, cycloalkylalkyl, arylalkyl or (heterocyclic)alkyl; and X is -C(=O)-, -C(=N-OH)-, -C(=N-CN)- or $-S(O)_2-$.

More preferred compounds of the invention are compounds of the formula **A** or **B** wherein R_1 is loweralkyl, benzyl, alkoxy-substituted benzyl or halo-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is loweralkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, aryl or arylalkyl; R_3 and R_4 are independently selected from loweralkyl, loweralkenyl, cycloalkylalkyl, benzyl, hydroxy-substituted benzyl, hydroxyalkyl-substituted benzyl, alkoxy-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substitutents are hydroxy and alkoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)-, -C(=N-OH)-, -C(=N-CN)- or $-S(O)_2-$.

Even more preferred compounds of the invention are compounds of the formula **A** or **B** wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is CH_3-, CH_3-$(CH_2)_2$-, $(CH_3)_2CHCH_2$-, $CH_3(CH_2)_3$-, $(CH_3(CH_2)_2)_2CH$-, cyclopentyl, $HOCH_2(CH_2)_3$-, $HOCH_2(CH_2)_2$- or $HOCH_2$-; R_3 and R_4 are independently selected from loweralkyl, allyl, cyclopropylmethyl, benzyl, hydroxy-substituted benzyl,

methoxy-substituted benzyl, hydroxymethyl-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substituents are hydroxy and methoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)- or -$S(O)_2$-.

Even more highly preferred compounds of the invention are compounds of the formula **A** or **B** wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is CH_3-, CH_3-$(CH_2)_2$-, $(CH_3)_2CHCH_2$-, $CH_3(CH_2)_3$-, $(CH_3(CH_2)_2)_2CH$-, cyclopentyl, $HOCH_2(CH_2)_3$-, $HOCH_2(CH_2)_2$- or $HOCH_2$-; R_3 and R_4 are independently selected from loweralkyl, allyl, cyclopropylmethyl, benzyl, hydroxy-substituted benzyl, methoxy-substituted benzyl, hydroxymethyl-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substituents are hydroxy and methoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)-.

Most highly preferred compounds of the invention are compounds of the formula **A** or **B** wherein R_1 is benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is CH_3-, CH_3-$(CH_2)_2$-, $(CH_3)_2CHCH_2$-, $CH_3(CH_2)_3$-, $(CH_3(CH_2)_2)_2CH$-, cyclopentyl, $HOCH_2(CH_2)_3$-, $HOCH_2(CH_2)_2$- or $HOCH_2$-; R_3 and R_4 are independently selected from loweralkyl, allyl, cyclopropylmethyl, benzyl, hydroxy-substituted benzyl, methoxy-substituted benzyl, hydroxymethyl-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substituents are hydroxy and methoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)-.

The especially preferred compounds of the invention are compounds of the formula **A** or **B** wherein R_1 is benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is $(CH_3)_2CHCH_2$-; R_3 and R_4 are independently selected from 4-hydroxybenzyl, 4-aminobenzyl and 3-aminobenzyl; and X is -C(=O)-.

The compounds of the invention comprise asymmetrically substituted centers (i.e., asymmetrically substituted carbon atoms). The present invention is intended to include all stereoisomeric forms of the compounds, including

racemic mixtures, mixtures of diastereomers, as well as single diastereomers of the compounds of the invention. The terms "S" and "R" configuration are as defined by the IUPAC 1974 Recommendations for Section E, Fundamental Stereochemistry, Pure Appl. Chem. (1976) 45, 13 - 30.

The term "N-protecting group" or "N-protected" as used herein refers to those groups intended to protect the N-terminus of an amino acid or peptide or to protect an amino group against undesirable reactions during synthetic procedures. Commonly used N-protecting groups are disclosed in Greene, "Protective Groups In Organic Synthesis," (John Wiley & Sons, New York (1981)), which is hereby incorporated herein by reference. N-protecting groups comprise acyl groups such as formyl, acetyl, propionyl, pivaloyl, t-butylacetyl, 2-chloroacetyl, 2-bromoacetyl, trifluoroacetyl, trichloroacetyl, phthalyl, o-nitrophenoxyacetyl, α-chlorobutyryl, benzoyl, 4-chlorobenzoyl, 4-bromobenzoyl, 4-nitrobenzoyl, and the like; sulfonyl groups such as benzenesulfonyl, p-toluenesulfonyl and the like; carbamate forming groups such as benzyloxycarbonyl, p-chlorobenzyloxycarbonyl, p-methoxybenzyloxycarbonyl, p-nitrobenzyloxycarbonyl, 2-nitrobenzyloxycarbonyl, p-bromobenzyloxycarbonyl, 3,4-dimethoxybenzyloxycarbonyl, 3,5-dimethoxybenzyloxycarbonyl, 2,4-dimethoxybenzyloxycarbonyl, 4-methoxybenzyloxycarbonyl, 2-nitro-4,5-dimethoxybenzyloxycarbonyl, 3,4,5-trimethoxybenzyloxycarbonyl, 1-(p-biphenylyl)-1-methylethoxycarbonyl, α,α-dimethyl-3,5-dimethoxybenzyloxycarbonyl, benzhydryloxycarbonyl, t-butyloxycarbonyl, diisopropylmethoxycarbonyl, isopropyloxycarbonyl, ethoxycarbonyl, methoxycarbonyl, allyloxycarbonyl, 2,2,2,-trichloroethoxycarbonyl, phenoxycarbonyl, 4-nitrophenoxycarbonyl, fluorenyl-9-methoxycarbonyl, cyclopentyloxycarbonyl, adamantyloxycarbonyl, cyclohexyloxycarbonyl, phenylthiocarbonyl and the like; alkyl groups such as benzyl, triphenylmethyl, benzyloxymethyl and the like; and silyl groups such as trimethylsilyl and the like. Preferred N-protecting groups are formyl, acetyl, benzoyl, pivaloyl, t-butylacetyl, phenylsulfonyl, benzyl, t-butyloxycarbonyl (Boc) and benzyloxycarbonyl (Cbz).

The term "O-protecting group" as used herein refers to a substituent which protects hydroxyl groups against undesirable reactions during synthetic

procedures such as those O-protecting groups disclosed in Greene, "Protective Groups In Organic Synthesis," (John Wiley & Sons, New York (1981)). O-protecting groups comprise substituted methyl ethers, for example, methoxymethyl, benzyloxymethyl, 2-methoxyethoxymethyl, 2-(trimethylsilyl)ethoxymethyl, t-butyl, benzyl and triphenylmethyl; tetrahydropyranyl ethers; substituted ethyl ethers, for example, 2,2,2-trichloroethyl; silyl ethers, for example, trimethylsilyl, t-butyldimethylsilyl and t-butyldiphenylsilyl; and esters prepared by reacting the hydroxyl group with a carboxylic acid, for example, acetate, propionate, benzoate and the like.

The term "loweralkyl" as used herein refers to straight or branched chain alkyl radicals containing from 1 to 10 carbon atoms including, but not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, n-pentyl, 1-methylbutyl, 2,2-dimethylbutyl, 2-methylpentyl, 2,2-dimethylpropyl, n-hexyl and the like.

The term "alkylene" as used herein refers to a straight or branched chain carbon diradical containing from 1 to 6 carbon atoms including, but not limited to, $-CH_2-$, $-CH_2CH_2-$, $-CH(CH_3)CH_2-$, $-CH_2CH_2CH_2-$ and the like.

The term "loweralkenyl" as used herein refers to a loweralkyl radical which contains at least one carbon-carbon double bond including, but not limited to, propenyl, butenyl and the like.

The term "aryl" as used herein refers to a C_6 monocyclic aromatic ring system or a C_9 or C_{10} bicyclic carbocyclic ring system having one or two aromatic rings including, but not limited to, phenyl, naphthyl, tetrahydronaphthyl, indanyl, indenyl and the like. Aryl groups can be unsubstituted or substituted with one, two or three substituents independently selected from loweralkyl, haloalkyl, alkoxy, thioalkoxy, alkoxycarbonyl, alkanoyl, hydroxy, halo, mercapto, nitro, cyano, amino, alkylamino, dialkylamino, carboxaldehyde, carboxy, carboxamide, arylalkyl, arylalkoxy, (heterocyclic)alkyl, (heterocyclic)alkoxy, (heterocyclic)carbonylalkoxy, aminoalkyl, aminoalkoxy, alkylaminoalkyl, alkylaminoalkoxy, dialkylaminoalkyl, dialkylaminoalkoxy, (alkoxyalkyl)aminoalkyl, (alkoxyalkyl)aminoalkoxy, di-(alkoxyalkyl)aminoalkyl, di-(alkoxyalkyl)aminoalkoxy, (alkoxyalkyl)(alkyl)aminoalkyl, (alkoxyalkyl)(alkyl)aminoalkoxy, hydroxyalkyl, hydroxyalkoxy, carboxyalkyl,

carboxyalkoxy, alkoxyalkyl, thioalkoxyalkyl, polyalkoxyalkyl and dialkoxyalkyl. In addition, substituted aryl groups include tetrafluorophenyl and pentafluorophenyl.

The term "arylalkyl" as used herein refers to an aryl group appended to a loweralkyl radical including, but not limited to, benzyl, 4-hydroxybenzyl, 1-naphthylmethyl and the like.

The term "aminoalkyl" as used herein refers to $-NH_2$ appended to a loweralkyl radical.

The term "hydroxyalkyl" as used herein refers to -OH appended to a loweralkyl radical.

The term "dihydroxyalkyl" as used herein refers to a loweralkyl radical disubstituted with -OH groups.

The term "polyhydroxyalkyl" as used herein refers to a loweralkyl radical substituted with more than two -OH groups.

The term "mercaptoalkyl" as used herein refers to a loweralkyl radical to which is appended a mercapto (-SH) group.

The term "hydroxyaminoalkyl" as used herein refers to a hydroxyamino group (-NHOH) appended to a loweralkyl radical.

The term "alkoxyaminoalkyl" as used herein refers to $-NHR_{20}$ (wherein R_{20} is an alkoxy group) appended to a loweralkyl radical.

The term "(alkoxy)(alkyl)aminoalkyl" as used herein refers to $(R_{21})(R_{22})N-$ wherein R_{21} is alkoxy and R_{22} is loweralkyl appended to a loweralkyl radical.

The term "alkylamino" as used herein refers to a loweralkyl radical appended to an NH radical.

The term "cycloalkyl" as used herein refers to an aliphatic ring having 3 to 7 carbon atoms including, but not limited to, cyclopropyl, cyclopentyl, cyclohexyl and the like. Cycloalkyl groups can be unsubstituted or substituted with one or two substituents independently selected from loweralkyl, haloalkyl, alkoxy, thioalkoxy, amino, alkylamino, dialkylamino, hydroxy, halo, mercapto, nitro, carboxaldehyde, carboxy, carboalkoxy and carboxamide.

The term "cycloalkylalkyl" as used herein refers to a cycloalkyl group appended to a loweralkyl radical, including but not limited to cyclohexylmethyl.

The term "cycloalkenyl" as used herein refers to an aliphatic ring having 5 to 7 carbon atoms and a carbon-carbon double bond including, but not limited to, cyclopentenyl, cyclohexenyl and the like. Cycloalkenyl groups can be unsubstituted or substituted with one or two substituents independently selected from loweralkyl, haloalkyl, alkoxy, thioalkoxy, amino, alkylamino, dialkylamino, hydroxy, halo, mercapto, nitro, carboxaldehyde, carboxy, carboalkoxy and carboxamide.

The term "cycloalkenylalkyl" as used herein refers to a cycloalkenyl group appended to a loweralkyl radical, including but not limited to cyclohexenylmethyl.

The term "alkylaminocycloalkyl" as used herein refers to an alkylamino group appended to a cycloalkyl radical.

The term "dialkylaminocycloalkyl" as used herein refers to a dialkylamino group appended to a cycloalkyl radical.

The terms "alkoxy" and "thioalkoxy" as used herein refer to $R_{29}O$- and $R_{29}S$-, respectively, wherein R_{29} is a loweralkyl group.

The term "alkoxyalkyl" as used herein refers to an alkoxy group appended to a loweralkyl radical.

The term "thioalkoxyalkyl" as used herein refers to a thioalkoxy group appended to a loweralkyl radical.

The term "guanidinoalkyl" as used herein refers to a guanidino group (-NHC(=NH)NH_2) appended to a loweralkyl radical.

The term "alkenyloxy" as used herein refers to $R_{32}O$- wherein R_{32} is a loweralkenyl group.

The term "hydroxyalkoxy" as used herein refers to -OH appended to an alkoxy radical.

The term "dihydroxyalkoxy" as used herein refers to an alkoxy radical which is disubstituted with -OH groups.

The term "arylalkoxy" as used herein refers $R_{33}O$- wherein R_{33} is a arylalkyl group as defined above.

The term "(heterocyclic)alkoxy" as used herein refers to $R_{34}O$- wherein R_{34} is a (heterocyclic)alkyl group.

The term "aryloxyalkyl" as used herein refers to a $R_{35}O$- group appended to a loweralkyl radical, wherein R_{35} is an aryl group.

The term "dialkylamino" as used herein refers to $-NR_{36}R_{37}$ wherein R_{36} and R_{37} are independently selected from loweralkyl groups.

The term "N-protected aminoalkyl" as used herein refers to $-NHR_{40}$ appended to a loweralkyl group, wherein R_{40} is an N-protecting group.

The term "alkylaminoalkyl" as used herein refers to $-NHR_{41}$ appended to a loweralkyl radical, wherein R_{41} is a loweralkyl group.

The term "(N-protected)(alkyl)aminoalkyl" as used herein refers to $-NR_{42}R_{43}$, which is appended to a loweralkyl radical, wherein R_{42} is an N-protecting group and R_{43} is loweralkyl.

The term "dialkylaminoalkyl" as used herein refers to $-NR_{44}R_{45}$ which is appended to a loweralkyl radical wherein R_{44} and R_{45} are independently selected from loweralkyl.

The term "carboxyalkyl" as used herein refers to a carboxylic acid group (-COOH) appended to a loweralkyl radical.

The term "alkoxycarbonylalkyl" as used herein refers to a $R_{46}C(O)$- group appended to a loweralkyl radical, wherein R_{46} is an alkoxy group .

The term "carboxyalkoxyalkyl" as used herein refers to a carboxylic acid group (-COOH) appended to an alkoxy group which is appended to a loweralkyl radical.

The term "alkoxycarbonylalkoxyalkyl" as used herein refers to an alkoxycarbonyl group ($R_{47}C(O)$- wherein R_{47} is an alkoxy group) appended to an alkoxy group which is appended to a loweralkyl radical.

The term "(amino)carboxyalkyl" as used herein refers to a loweralkyl radical to which is appended a carboxylic acid group (-COOH) and an amino group ($-NH_2$).

The term "((N-protected)amino)carboxyalkyl" as used herein refers to a loweralkyl radical to which is appended a carboxylic acid group (-COOH) and $-NHR_{48}$ wherein R_{48} is an N-protecting group.

The term "(alkylamino)carboxyalkyl" as used herein refers to a loweralkyl radical to which is appended a carboxylic acid group (-COOH) and an alkylamino group.

The term "((N-protected)alkylamino)carboxyalkyl" as used herein refers to a loweralkyl radical to which is appended a carboxylic acid group (-COOH) and an $-NR_{48}R_{49}$ wherein R_{48} is as defined above and R_{49} is a loweralkyl group.

The term "(dialkylamino)carboxyalkyl" as used herein refers to a loweralkyl radical to which is appended a carboxylic acid group (-COOH) and $-NR_{49}R_{49}$ wherein R_{49} is as defined above.

The term "(amino)alkoxycarbonylalkyl" as used herein refers to a loweralkyl radical to which is appended an alkoxycarbonyl group as defined above and an amino group ($-NH_2$).

The term "((N-protected)amino)alkoxy-carbonylalkyl" as used herein refers to a loweralkyl radical to which is appended an alkoxycarbonyl group as defined above and $-NHR_{50}$ wherein R_{50} is an N-protecting group.

The term "(alkylamino)alkoxycarbonylalkyl" as used herein refers to a loweralkyl radical to which is appended an alkoxycarbonyl group as defined above and an alkylamino group as defined above.

The term "((N-protected)alkylamino)alkoxy-carbonylalkyl" as used herein refers to a loweralkyl radical to which is appended an alkoxycarbonyl group as defined above and $-NR_{51}R_{52}$ wherein R_{51} is an N-protecting group and R_{52} is a loweralkyl group.

The term "(dialkylamino)alkoxycarbonylalkyl" as used herein refers to a loweralkyl radical to which is appended an alkoxycarbonyl group as defined above and $-NR_{53}R_{54}$ wherein R_{53} and R_{54} are independently selected from loweralkyl.

The term "aminocycloalkyl" as used herein refers to an NH_2 appended to a cycloalkyl radical.

The term "((alkoxy)alkoxy)alkyl" as used herein refers to an alkoxy group appended to an alkoxy group which is appended to a loweralkyl radical.

The term "polyalkoxyalkyl" as used herein refers to a polyalkoxy residue appended to a loweralkyl radical.

The term "polyalkoxy" as used herein refers to $-OR_{67}$ wherein R_{67} is a straight or branched chain containing 1-5, $C_{n'}$-O-$C_{n''}$ linkages wherein n' and n" are independently selected from 1 to 3, including but not limited to methoxyethoxymethoxy, methoxymethoxy and the like.

The term "halo" or "halogen" as used herein refers to -Cl, -Br, -I or -F.

The term "haloalkyl" as used herein refers to a loweralkyl radical in which one or more of the hydrogen atoms are replaced by halogen including, but not limited to, chloromethyl, trifluoromethyl, 1-chloro-2-fluoroethyl and the like.

The term "thioalkoxyalkyl" as used herein refers to a thioalkoxy group appended to a loweralkyl radical.

The term "alkylsulfonyl" as used herein refers to $R_{93}SO_2$- wherein R_{93} is loweralkyl group.

The term "alkylsulfonylalkyl" as used herein refers to an alkylsufonyl group appended to a loweralkyl radical.

The term "arylthioalkyl" as used herein refers to R_{94}-S-R_{95}- wherein R_{94} is an aryl group and R_{95} is an alkylene group.

The term "aryloxyalkyl" as used herein refers to R_{94}-O-R_{95}- wherein R_{94} is an aryl group and R_{95} is an alkylene group.

The term "arylsulfonylalkyl" as used herein refers to R_{96}-S(O)$_2$-R_{97}- wherein R_{96} is any aryl group and R_{97} is an alkylene group.

The term "(heterocyclic)oxyalkyl" as used herein refers to R_{98}-O-R_{99}- wherein R_{98} is a heterocyclic group and R_{99} is an alkylene group.

The term "(heterocyclic)thioalkyl" as used herein refers to R_{100}-S-R_{101}- wherein R_{100} is a heterocyclic group and R_{101} is an alkylene group.

The term "(heterocyclic)sulfonylalkyl" as used herein refers to R_{102}-S(O)$_2$-R_{103}- wherein R_{102} is a heterocyclic group and R_{103} is an alkylene group.

The "arylalkoxyalkyl" as used herein refers to R_{104}-O-R_{105}- wherein R_{104} is an arylalkyl group and R_{105} is an alkylene group, for example, benzyloxymethyl and the like.

The "arylthioalkoxyalkyl" as used herein refers to R_{106}-S-R_{107}- wherein R_{106} is an arylalkyl group and R_{107} is an alkylene group.

The "arylalkylsulfonylalkyl" as used herein refers to R_{108}-S(O)$_2$-R_{109}- wherein R_{108} is an arylalkyl group and R_{109} is an alkylene group.

The term "(heterocyclic)alkoxy" as used herein refers to R_{110}-O- wherein R_{110} is a (heterocyclic)alkyl group, for example, 2-(morpholin-1-yl)ethoxy and the like.

The term "(heterocyclic)alkoxyalkyl" as used herein refers to R_{110}-O-R_{111}- wherein R_{110} is a (heterocyclic)alkyl group and R_{111} is an alkylene group.

The term "(heterocyclic)thioalkoxyalkyl" as used herein refers to R_{112}-S-R_{113}- wherein R_{112} is a (heterocyclic)alkyl group and R_{113} is an alkylene group.

The term "(heterocyclic)alkylsulfonylalkyl" as used herein refers to R_{114}-S(O)$_2$-R_{115}- wherein R_{114} is a (heterocyclic)alkyl group and R_{115} is an alkylene group.

The term "cycloalkyloxyalkyl" as used herein refers to R_{116}-O-R_{117}- wherein R_{116} is a cycloalkyl group and R_{117} is an alkylene group.

The term "cycloalkylthioalkyl" as used herein refers to R_{118}-S-R_{119}- wherein R_{118} is a cycloalkyl group and R_{119} is an alkylene group.

The term "cycloalkylsulfonylalkyl" as used herein refers to R_{120}-S(O)$_2$-R_{121}- wherein R_{120} is a cycloalkyl group and R_{121} is an alkylene group.

The term "cycloalkylalkoxyalkyl" as used herein refers to R_{122}-O-R_{123}- wherein R_{122} is a cycloalkylalkyl group and R_{123} is an alkylene group.

The term "cycloalkylthioalkoxyalkyl" as used herein refers to R_{124}-S-R_{125}- wherein R_{124} is a cycloalkylalkyl group and R_{125} is an alkylene group.

The term "cycloalkylalkylsulfonylalkyl" as used herein refers to R_{126}-S(O)$_2$-R_{127}- wherein R_{126} is a cycloalkylalkyl group and R_{127} is an alkylene group.

The term "alkanoyl" as used herein refers to R_k-C(O)- wherein R_k is a loweralkyl group.

The term "aminocarbonyl" as used herein refers to -C(O)NH_2.

The term "aminocarbonylalkyl" as used herein refers to an aminocarbonyl group appended to a loweralkyl radical.

The term "alkylaminocarbonyl" as used herein refers to -C(O)NHR_{128} wherein R_{128} is loweralkyl.

The term "alkylaminocarbonylalkyl" as used herein refers to an alkylaminocarbonyl group appended to a loweralkyl radical.

The term "dialkylaminocarbonyl" as used herein refers to -C(O)$NR_{129}R_{130}$ wherein R_{129} and R_{130} are independently selected from loweralkyl.

The term "dialkylaminocarbonylalkyl" as used herein refers to a dialkylaminocarbonyl group appended to a loweralkyl group.

The term "aroylalkyl" as used herein refers to R_{131}-C(O)-R_{132}- wherein R_{131} is an aryl group and R_{132} is an alkylene group.

The term "(heterocyclic)carbonylalkyl" as used herein refers to R_{133}-C(O)-R_{134}- wherein R_{133} is a heterocyclic group and R_{134} is an alkylene group.

The term "aminoalkoxy" as used herein refers to an alkoxy radical to which is appended an amino (-NH_2) group.

The term "alkylaminoalkoxy" as used herein refers to an alkoxy radical to which is appended an alkylamino group.

The term "dialkylaminoalkoxy" as used herein refers to an alkoxy radical to which is appended a dialkylamino group.

The term "(alkoxyalkyl)aminoalkyl" refers to a loweralkyl radical to which is appended an (alkoxyalkyl)amino group.

The term "(alkoxyalkyl)aminoalkoxy" as used herein refers to an alkoxy radical to which is appended an (alkoxyalkyl)amino group.

The term "(alkoxyalkyl)(alkyl)aminoalkyl" refers to a loweralkyl radical to which is appended an (alkoxyalkyl)(alkyl)amino group.

The term "(alkoxyalkyl)(alkyl)aminoalkoxy" as used herein refers to an alkoxy radical to which is appended an (alkoxyalkyl)(alkyl)amino group.

The term "di-(alkoxyalkyl)aminoalkyl" refers to a loweralkyl radical to which is appended an di-(alkoxyalkyl)amino group.

The term "di-(alkoxyalkyl)aminoalkoxy" as used herein refers to an alkoxy radical to which is appended an di-(alkoxyalkyl)amino group.

The term "carboxyalkoxy" as used herein refers to an alkoxy radical to which is appended a carboxy (-COOH) group.

The term "aminocarbonylalkyl" as used herein refers to a loweralkyl radical to which is appended an aminocarbonyl ($H_2NC(O)$-) group.

The term "alkylaminocarbonylalkyl" as used herein refers to a loweralkyl radical to which is appended an alkylaminocarbonyl group.

The term "dialkylaminocarbonylalkyl" as used herein refers to a loweralkyl radical to which is appended an dialkylaminocarbonyl group.

The term "(heterocyclic)carbonylalkoxy" as used herein refers to R_{135}-C(O)-R_{136}-O- wherein R_{135} is a heterocyclic group and R_{136} is an alkylene group, for example, 2-(morpholin-1-yl-carbonyl)ethoxy and the like.

The term "arylalkoxycarbonylalkyl" as used herein refers to R_{137}-O-C(O)-R_{138}- wherein R_{137} is an arylalkyl group and R_{138} is an alkylene group.

The term "alkanoyl" as used herein refers to R_{139}-C(O)- wherein R_{139} is a loweralkyl group.

The term "aroyl" as used herein refers to R_{140}-C(O)- wherein R_{140} is an aryl group.

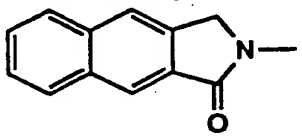
The term "alkylsulfonyl" as used herein refers to R_{141}-$S(O)_2$- wherein R_{141} is a loweralkyl group.

The term "arylsulfonyl" as used herein refers to R_{142}-$S(O)_2$- wherein R_{142} is an aryl group.

At each occurrence, the term "heterocyclic ring" or "heterocyclic" as used herein independently refers to a 3- or 4-membered ring containing a heteroatom selected from oxygen, nitrogen and sulfur; or a 5-, 6- or 7-membered ring containing one, two or three nitrogen atoms; one oxygen atom; one sulfur atom; one nitrogen and one sulfur atom; one nitrogen and one oxygen atom; two oxygen atoms in non-adjacent positions; one oxygen and one sulfur atom in

non-adjacent positions; or two sulfur atoms in non-adjacent positions. The 5-membered ring has 0-2 double bonds and the 6-membered ring has 0-3 double bonds. The nitrogen heteroatoms can be optionally quaternized or N-oxidized. The sulfur heteroatoms can be optionally S-oxidized. The term "heterocyclic" also includes bicyclic groups in which any of the above heterocyclic rings is fused to a benzene ring or a cyclohexane ring or another heterocyclic ring. Heterocyclics include: pyrrolyl, pyrrolinyl, pyrrolidinyl, pyrazolyl, pyrazolinyl, pyrazolidinyl, imidazolyl, imidazolinyl, imidazolidinyl, pyridyl, piperidinyl, pyrazinyl, piperazinyl, pyrimidinyl, pyridazinyl, oxazolyl, oxazolinyl, oxazolidinyl, isoxazolyl, isoxazolinyl, isoxazolidinyl, morpholinyl, thiazolyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, indolyl, quinolinyl, tetrahydroquinolyl, isoquinolinyl, benzimidazolyl, benzothiazolyl, benzoxazolyl, benzofuranyl, furanyl, dihydrofuranyl, tetrahydrofuranyl, pyranyl, dihydropyranyl, tetrahydropyranyl, dioxanyl, dioxolanyl, thienyl and benzothienyl.

Heterocyclics also include:



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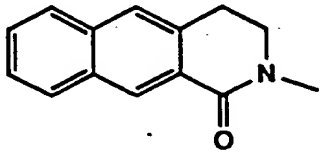

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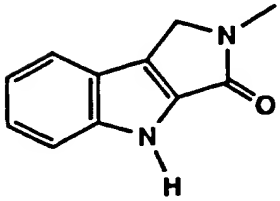

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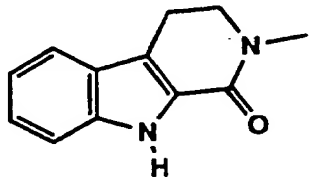


Preferred heterocyclics are pyridyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, furanyl, thienyl, tetrahydrofuranyl, tetrahydrothienyl and tetrahydropyranyl.

Heterocyclics can be unsubstituted or monosubstituted or disubstituted with substituents independently selected from hydroxy, halo, oxo (=O), alkylimino (R*N= wherein R* is a loweralkyl group), amino, (N-protected)amino, alkylamino, (N-protected)alkylamino, dialkylamino, alkoxy, polyalkoxy, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl,

-COOH, -SO_3H, loweralkenyl, loweralkyl, hydroxyalkyl, aminoalkyl and alkoxyalkyl. Heterocyclics can also be substituted with a heterocycle selected from aziridinyl, azetidinyl, pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, pyridinyl, pyrimidinyl, pyridazinyl and pyrazinyl, each of which can be unsubstituted or substituted with a substituent selected from halo, loweralkyl, hydroxy, alkoxy and thioalkoxy.

In addition, nitrogen containing heterocycles can be N-protected.

The term "(heterocyclic)alkyl" as used herein refers to a heterocyclic group appended to a loweralkyl radical, including but not limited to imidazolylmethyl, thiazolylmethyl, oxazolylmethyl, furanylmethyl, isoxazolylmethyl and the like.

The term "naturally occurring α-amino acid" as used herein refers to alanine, valine, leucine, isoleucine, proline, phenylalanine, tryptophan, methionine, glycine, serine, threonine, cysteine, tyrosine, asparagine, glutamine, aspartic acid, glutamic acid, lysine, arginine or histidine.

In the compounds of the invention, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

Most preferred compounds of the invention are selected from the group consisting of:

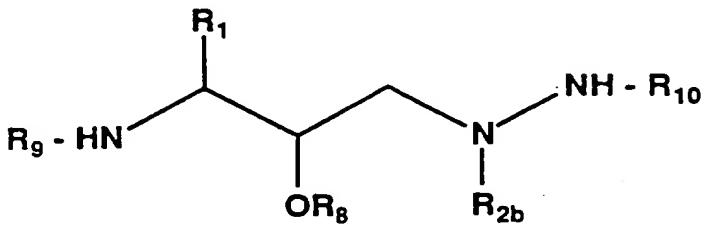
(5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane;

(5R,6R)-2,4-Bis-(3-aminobenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane; and

(5R,6R)-2,4-Bis-(4-aminobenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane;

or a pharmaceutically acceptable salt, ester or prodrug thereof.

Compounds useful as intermediates for the preparation of the compounds of formula **A** include the compound of the formula **C:**



C

wherein R_1 is selected from:

(i) hydrogen,
(ii) loweralkyl,
(iii) aryl,
(iv) thioalkoxyalkyl,
(v) (aryl)alkyl,
(vi) cycloalkyl,
(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,
(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,
(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,
(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,
(xx) loweralkenyl,
(xxi) heterocyclic,
(xxii) (heterocyclic)alkyl),
(xxiii) arylthioalkyl,

(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,
(xxvii) (heterocyclic)oxyalkyl,
(xxviii) arylalkoxyalkyl,
(xxix) arylthioalkoxyalkyl,
(xxx) arylalkylsulfonylalkyl,
(xxxi) (heterocyclic)alkoxyalkyl,
(xxxii) (heterocyclic)thioalkoxyalkyl,
(xxxiii) (heterocyclic)alkylsulfonylalkyl,
(xxxiv) cycloalkyloxyalkyl,
(xxxv) cycloalkylthioalkyl,
(xxxvi) cycloalkylsulfonylalkyl,
(xxxvii) cycloalkylalkoxyalkyl,
(xxxviii) cycloalkylthioalkoxyalkyl,
(xxxix) cycloalkylalkylsulfonylalkyl,
(xl) aminocarbonyl,
(xli) alkylaminocarbonyl,
(xlii) dialkylaminocarbonyl,
(xliii) aroylalkyl,
(xliv) (heterocyclic)carbonylalkyl,
(xlv) polyhydroxyalkyl,
(xlvi) aminocarbonylalkyl,
(xlvii) alkylaminocarbonylalkyl,
(xlviii) dialkylaminocarbonylalkyl,
(xlix) aryloxyalkyl,
(l) alkylsulfonylalkyl and
(li) arylalkoxycarbonylalkyl;

R_{2b} is selected from:

(i) hydrogen,
(ii) benzyl,
(iii) nitrobenzyl,
(iv) dimethoxybenzyl,

(v) diphenylmethyl,
(vi) di-(methoxyphenyl)methyl and
(vii) triphenylmethyl;

R_8 is hydrogen or an O-protecting group; and
R_9 and R_{10} are independently selected from hydrogen and an N-protecting group; or an acid addition salt thereof.

Preferred compounds of the formula **C** are those wherein R_1 is loweralkyl or arylalkyl and R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

A preferred N-protecting group R_9 is t-butyloxycarbonyl or benzyloxycarbonyl.

A preferred N-protecting group R_{10} is t-butyloxycarbonyl or benzyloxycarbonyl.

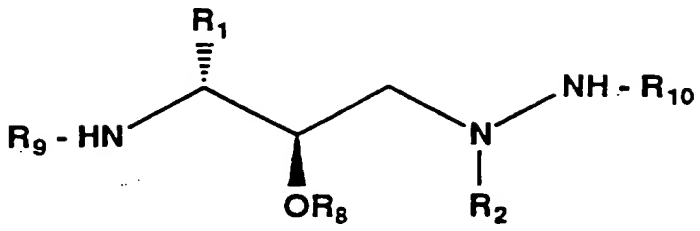
More preferred compounds are compounds of the formula **C** wherein R_1 is loweralkyl, benzyl, alkoxy-substituted benzyl or halo-substituted benzyl; and R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

Even more preferred compounds of the formula **C** are those wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

Even more highly preferred compounds are compounds of the formula **C** wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; and R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

Most highly preferred compounds are compounds of the formula **C** wherein R_1 is benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; and R_2 is R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

Preferred compounds of the formula **C** also include compounds of the formula **D**:



D

wherein R_1 is selected from:

(i) hydrogen,
(ii) loweralkyl,
(iii) aryl,
(iv) thioalkoxyalkyl,
(v) (aryl)alkyl,
(vi) cycloalkyl,
(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,
(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,
(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,
(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,
(xx) loweralkenyl,
(xxi) heterocyclic,
(xxii) (heterocyclic)alkyl),

(xxiii) arylthioalkyl,
(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,
(xxvii) (heterocyclic)oxyalkyl,
(xxviii) arylalkoxyalkyl,
(xxix) arylthioalkoxyalkyl,
(xxx) arylalkylsulfonylalkyl,
(xxxi) (heterocyclic)alkoxyalkyl,
(xxxii) (heterocyclic)thioalkoxyalkyl,
(xxxiii) (heterocyclic)alkylsulfonylalkyl,
(xxxiv) cycloalkyloxyalkyl,
(xxxv) cycloalkylthioalkyl,
(xxxvi) cycloalkylsulfonylalkyl,
(xxxvii) cycloalkylalkoxyalkyl,
(xxxviii) cycloalkylthioalkoxyalkyl,
(xxxix) cycloalkylalkylsulfonylalkyl,
(xl) aminocarbonyl,
(xli) alkylaminocarbonyl,
(xlii) dialkylaminocarbonyl,
(xliii) aroylalkyl,
(xliv) (heterocyclic)carbonylalkyl,
(xlv) polyhydroxyalkyl,
(xlvi) aminocarbonylalkyl,
(xlvii) alkylaminocarbonylalkyl,
(xlviii) dialkylaminocarbonylalkyl,
(xlix) aryloxyalkyl,
(l) alkylsulfonylalkyl and
(li) arylalkoxycarbonylalkyl;

R_{2b} is selected from:

(i) hydrogen,
(ii) benzyl,
(iii) nitrobenzyl,

(iv) dimethoxybenzyl,
(v) diphenylmethyl,
(vi) di-(methoxyphenyl)methyl and
(vii) triphenylmethyl;

R_8 is hydrogen or an O-protecting group; and
R_9 and R_{10} are independently selected from hydrogen and an N-protecting group; or an acid addition salt thereof.

Preferred compounds of the formula **D** are those wherein R_1 is loweralkyl or arylalkyl and R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

A preferred N-protecting group R_9 is t-butyloxycarbonyl or benzyloxycarbonyl.

A preferred N-protecting group R_{10} is t-butyloxycarbonyl or benzyloxycarbonyl.

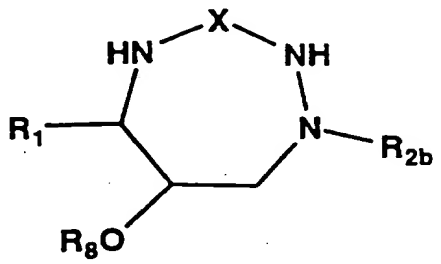
More preferred compounds are compounds of the formula **D** wherein R_1 is loweralkyl, benzyl, alkoxy-substituted benzyl or halo-substituted benzyl; R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

Even more preferred compounds of the formula **D** are those wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

Even more highly preferred compounds are compounds of the formula **D** wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; and R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

Most highly preferred compounds are compounds of the formula **D** wherein R_1 is benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; and R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

Other compounds which are useful as intermediates for the preparation of the compounds of formula **A** include the compound of the formula **E**:



E

wherein R_1 is selected from:

(i) hydrogen,
(ii) loweralkyl,
(iii) aryl,
(iv) thioalkoxyalkyl,
(v) (aryl)alkyl,
(vi) cycloalkyl,
(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,
(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,
(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,
(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,
(xx) loweralkenyl,
(xxi) heterocyclic,

(xxii) (heterocyclic)alkyl),
(xxiii) arylthioalkyl,
(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,
(xxvii) (heterocyclic)oxyalkyl,
(xxviii) arylalkoxyalkyl,
(xxix) arylthioalkoxyalkyl,
(xxx) arylalkylsulfonylalkyl,
(xxxi) (heterocyclic)alkoxyalkyl,
(xxxii) (heterocyclic)thioalkoxyalkyl,
(xxxiii) (heterocyclic)alkylsulfonylalkyl,
(xxxiv) cycloalkyloxyalkyl,
(xxxv) cycloalkylthioalkyl,
(xxxvi) cycloalkylsulfonylalkyl,
(xxxvii) cycloalkylalkoxyalkyl,
(xxxviii) cycloalkylthioalkoxyalkyl,
(xxxix) cycloalkylalkylsulfonylalkyl,
(xl) aminocarbonyl,
(xli) alkylaminocarbonyl,
(xlii) dialkylaminocarbonyl,
(xliii) aroylalkyl,
(xliv) (heterocyclic)carbonylalkyl,
(xlv) polyhydroxyalkyl,
(xlvi) aminocarbonylalkyl,
(xlvii) alkylaminocarbonylalkyl,
(xlviii) dialkylaminocarbonylalkyl,
(xlix) aryloxyalkyl,
(l) alkylsulfonylalkyl and
(li) arylalkoxycarbonylalkyl;

R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl;

R_8 is hydrogen or an O-protecting group; and

X is

(i) -C(=Y)- wherein Y is O, S or N(R_5) wherein R_5 is loweralkyl, hydroxy, amino, alkylamino, dialkylamino, alkoxy, benzyloxy, cyano or nitro;

(ii) -S(O)- or

(iii) -$S(O)_2$-;

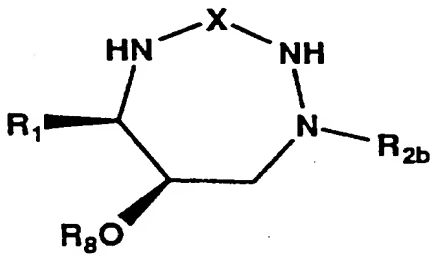
or a salt thereof.

Preferred compounds of the formula **E** are those wherein R_1 is loweralkyl or arylalkyl; R_{2b} is benzyl and R_8 is an O-protecting group.

More preferred compounds are compounds of the formula **E** wherein R_1 is loweralkyl, benzyl, alkoxy-substituted benzyl or halo-substituted benzyl and X is -C(=O)-.

Even more preferred compounds of the formula **E** are those wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl and X is -C(=O)-.

Preferred compounds of formula **E** also include compounds of the formula **F**:



F

wherein R_1 is selected from:

(i) hydrogen,

(ii) loweralkyl,

(iii) aryl,

(iv) thioalkoxyalkyl,

(v) (aryl)alkyl,

(vi) cycloalkyl,

(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,
(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,
(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,
(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,
(xx) loweralkenyl,
(xxi) heterocyclic,
(xxii) (heterocyclic)alkyl),
(xxiii) arylthioalkyl,
(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,
(xxvii) (heterocyclic)oxyalkyl,
(xxviii) arylalkoxyalkyl,
(xxix) arylthioalkoxyalkyl,
(xxx) arylalkylsulfonylalkyl,
(xxxi) (heterocyclic)alkoxyalkyl,
(xxxii) (heterocyclic)thioalkoxyalkyl,
(xxxiii) (heterocyclic)alkylsulfonylalkyl,
(xxxiv) cycloalkyloxyalkyl,
(xxxv) cycloalkylthioalkyl,
(xxxvi) cycloalkylsulfonylalkyl,
(xxxvii) cycloalkylalkoxyalkyl,
(xxxviii) cycloalkylthioalkoxyalkyl,
(xxxix) cycloalkylalkylsulfonylalkyl,
(xl) aminocarbonyl,

(xli) alkylaminocarbonyl,
(xlii) dialkylaminocarbonyl,
(xliii) aroylalkyl,
(xliv) (heterocyclic)carbonylalkyl,
(xlv) polyhydroxyalkyl,
(xlvi) aminocarbonylalkyl,
(xlvii) alkylaminocarbonylalkyl,
(xlviii) dialkylaminocarbonylalkyl,
(xlix) aryloxyalkyl,
(l) alkylsulfonylalkyl and
(li) arylalkoxycarbonylalkyl;

R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl;

R_8 is hydrogen or an O-protecting group; and
X is

(i) -C(=Y)- wherein Y is O, S or N(R_5) wherein R_5 is loweralkyl, hydroxy, amino, alkylamino, dialkylamino, alkoxy, benzyloxy, cyano or nitro;
(ii) -S(O)- or
(iii) -$S(O)_2$-;

or a salt thereof.

Preferred compounds of the formula **F** are those wherein R_1 is loweralkyl or arylalkyl; R_{2b} is benzyl and R_8 is an O-protecting group.

More preferred compounds are compounds of the formula **F** wherein R_1 is loweralkyl, benzyl, alkoxy-substituted benzyl or halo-substituted benzyl and X is -C(=O)-.

Even more preferred compounds of the formula **F** are those wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl and X is -C(=O)-.

The compounds of the invention can be prepared as shown in Schemes 1 - 5. The schemes outline the preparation of the compounds of the invention having the preferred stereochemistry. However, other stereoisomers of the compounds of the invention can be prepared by starting with the aminoalcohol

having the opposite stereochemistry to that shown for compound **1** in Scheme 1. As outlined in Scheme 1, oxidation (for example, Swern oxidation) of (D)-aminoalcohol **1** (R_9 is an N-protecting group, for example, benzyloxycarbonyl and R_1 is defined as above) provides aldehyde **2**. Olefination (for example, by Wittig reaction) of N-protected aldehyde **2** provides olefin **3**. Epoxidation of olefin **3** (for example, with m-chloroperbenzoic acid (MCPBA)) provides a mixture of epoxides **4** and **5**. Separation of the epoxides (for example, by chromatography) provides the desired epoxide isomer **4**.

As outlined in Scheme 2, reaction of N-protected hydrazine **6** (R_{10} is an N-protecting group, for example, benzyloxycarbonyl) with an aldehyde or ketone derivative of substituent R_{2b} provides hydrazone **7**. Reduction of hydrazone **7** (for example, by hydrogenation) provides hydrazine **8**.

Alternatively, the appropriate hydrazine R_{2b}-NH-NH_2 can be N-protected to provide **8**.

As outlined in Scheme 3, reaction of epoxide **4** with hydrazine **8** provides hydroxy hydrazine **9**. Protection of the hydroxyl group with an O-protecting group (for example, trimethylsilylethoxymethyl, methoxyethoxymethyl or methoxymethyl and the like) provides **10**. Removal of N-protecting groups provides **11**.

As outlined in Scheme 4, reaction of **11** with Q-X-Q' (Q and Q' are activating groups and X is defined as above) provides **12**. When X is -C(=O)- or -C(=S)-, Q and Q" are, for example, independently selected from imidazolyl, N-succinimidyloxy, -O-phenyl, halogen and the like. When X is -C(=N-CN)-, Q-X-Q' is, for example, MeS-C(=N-CN)-SMe and the like. When X is -S(O)- or -$S(O)_2$-, Q and Q' are, for example, imidazolyl and the like. Compounds wherein X is -C(=N-R_5)- wherein R_5 is loweralkyl, hydroxy, amino, alkylamino, dialkylamino, alkoxy or benzyloxy can be prepared by reacting the appropriate amine with the corresponding cyclic thiourea.

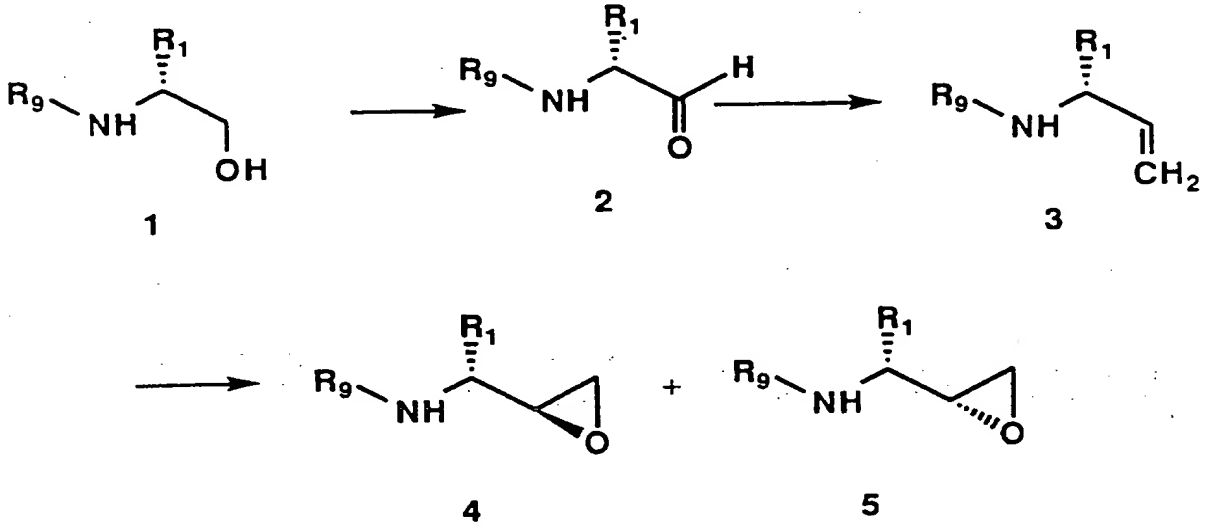
Alkylation of **12** with R_3-Z and R_4-Z' wherein Z and Z' are independently selected from leaving groups, for example, a sulfonate (mesylate, tosylate, triflate and the like) or a halogen and the like, provides **13**. When R_3 and R_4 are the same, the alkylation can be done in one step. When R_3 and R_4 are different, the alkylations are done sequentially (the R_4 substituent being introduced first,

followed by the R_3 substituent). Deprotection of the hydroxyl group then provides **14**.

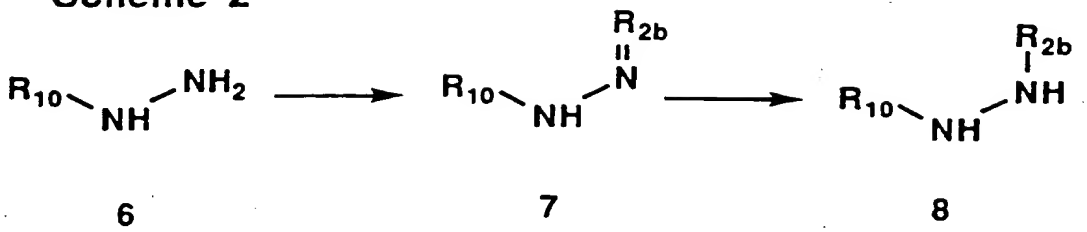
As outlined in Scheme 5, various substituents R_2 can be introduced by first removing the N-protecting group R_{2b} from compound **12** (by hydrogenation or other suitable N-debenzylation method) to give **13**. Acylation or sulfonylation of **13** with R_2-Z wherein R_2-Z is a carboxylic acid halide or sulfonyl halide and the like provides **14**.

Alkylation of **14** with R_3-Z' and R_4-Z" wherein Z' and Z" are independently selected from leaving groups, for example, a sulfonate (mesylate, tosylate, triflate and the like) or a halogen and the like, provides **15**. When R_3 and R_4 are the same, the alkylation can be done in one step. When R_3 and R_4 are different, the alkylations are done sequentially (the R_4 substituent being introduced first, followed by the R_3 substituent). Deprotection of the hydroxyl group then provides **16**.

Scheme 1

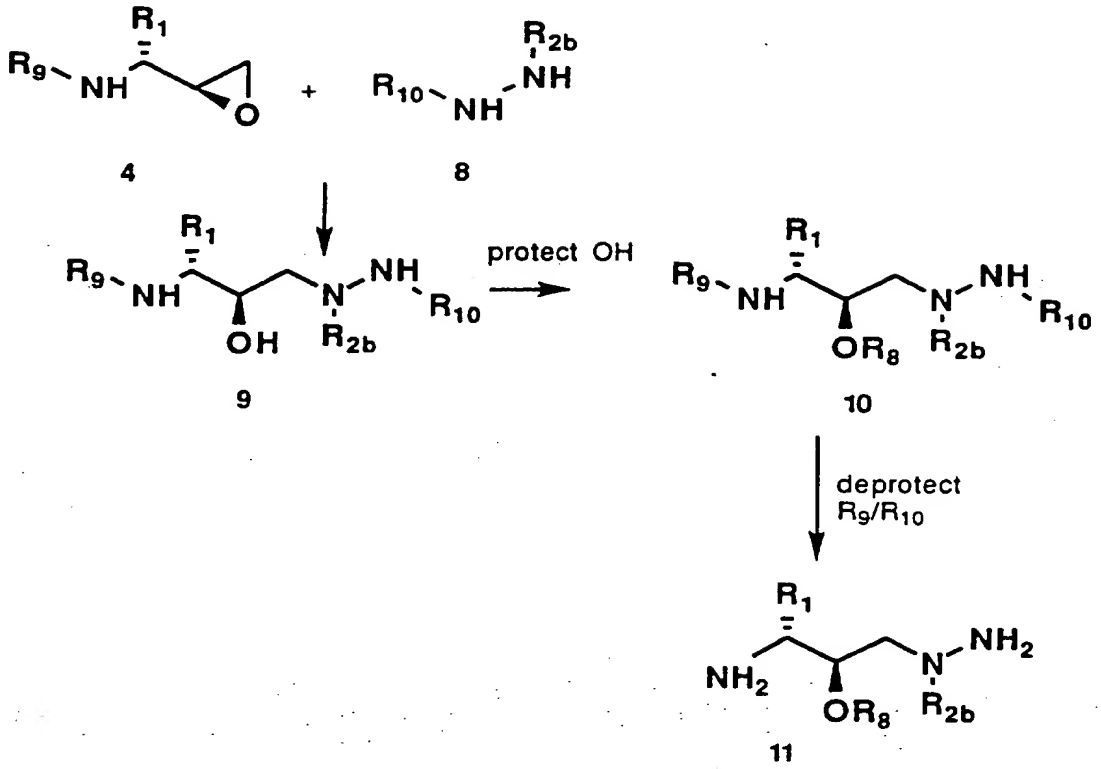


Scheme 2

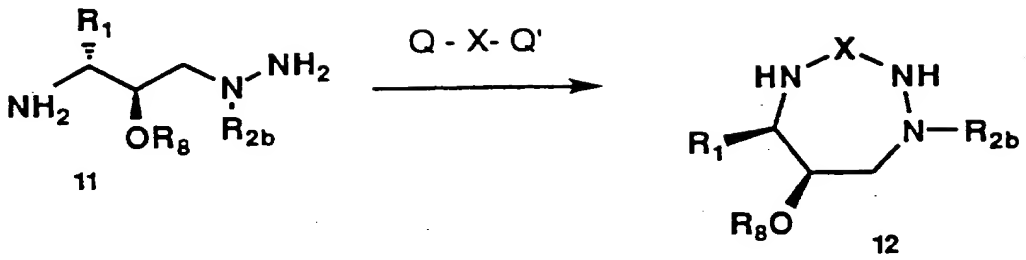


6 7 8

Scheme 3

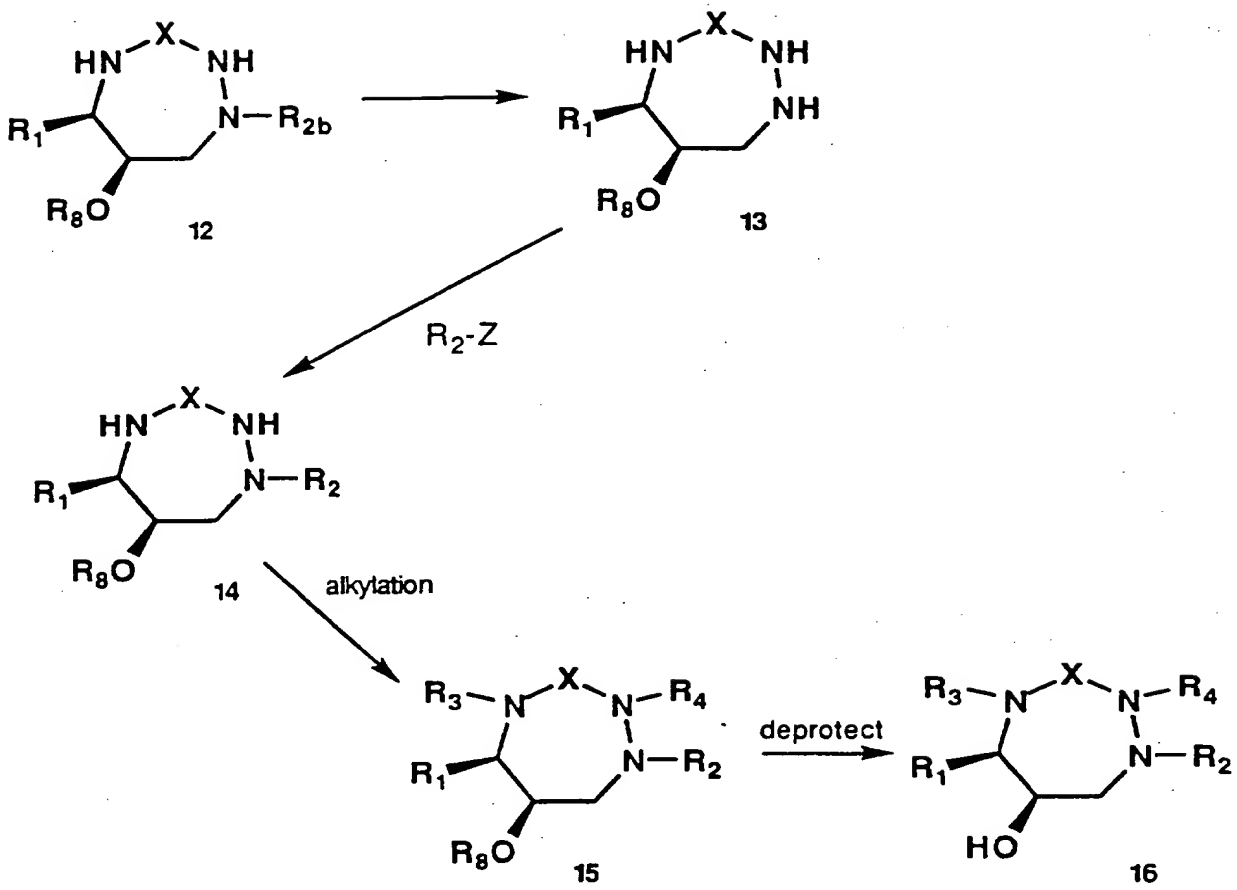


Scheme 4



11 12

Scheme 5



The following examples will serve to further illustrate the preparation of the novel compounds of the invention.

Example 1

A. N-((Benzyloxy)carbonyl)-D-phenylalaninal.

To a solution of 1.8 ml of dimethyl sulfoxide in 20 ml of dichloromethane cooled to -78°C was added slowly 1.65 ml of oxalyl chloride. The solution was stirred for 10 min at -78°C and a solution of 3.6 g (0.012 mole) of N-((benzyloxy)carbonyl)-D-phenylalaninol in 45 ml of dichloromethane was added slowly. The resulting solution was stirred at -78°C for 15 min, then 1 min at 0°C; recooling to -78°C and 7.6 ml of triethylamine was added over 10 min. After stirring at -78°C for 25 min, 20 ml of cold 10% aq. citric acid solution was added. After warming to 0°C, 200 ml of ether and 55 ml of cold 10% citric acid were added. The organic layer was separated by separatory funnel and washed repeatedly (5 x 60 ml) with water and finally with satd. NaCl solution. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo* at RT to give 3.51 g of the desired compound as an off-white solid.

B. N((Benzyloxy)carbonyl)-2R-amino-1-phenyl-but-3-ene.

To a dry 250 ml 3-neck flask was added 14.34 g of triphenylmethylphosphonium bromide. To this was added 70 ml of THF, cooled to 0°C and 4.42 g of 35% potassium hydride dispersion in oil was added. The mixture was stirred at RT for 24 h. To this mixture was added 30 ml of toluene and let stand for 30 min. The supernatant was cannulated over into a solution of 3.37 g of N-((benzyloxy)carbonyl)-D-phenylalaninal in 50 ml of toluene at -78°C. The reaction mixture was stirred at -78°C for 2 h, followed by 0.5 h at RT. Satd. ammonium chloride (50 ml) was added. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 x 100 ml). The combined organic layer was washed with satd. NaCl solution and dried over anhydrous sodium sulfate, filtered and concentrated to a yellow oil which was purified by silica gel column chromatography (30% ether/hexane) to provide 3.02 g (89%) of desired compound as a white solid. ^{1}H NMR ($CDCl_3$): δ 2.88 (d, 2H), 4.50 (m, 1H), 4.70 (m, 1H), 5.10 (m, 3H), 5.80 (m, 1H), 7.10-7.40 (m, 10H). Mass spectrum: $(M+1)^+$ = 282.

C. N-((Benzyloxy)carbonyl)-2R-amino-3S-3,4-epoxybutane.

According to the procedure of Luly, *et al.* (J. Org. Chem. 52, 1487 (1987)), to a solution of 2.97 g of the product of Example 1B in 75 ml of dichloromethane at 0°C was added 9 g of MCPBA. The solution was stirred at 0°C for 1 h and then at RT overnight. It was added to 250 ml of ether and washed successively with cold 10% sodium thiosulfate, 10% sodium carbonate and then satd. NaCl solution. The organic layer was dried and concentrated to a colorless oil which was purified by silica gel column chromatography (20% EtOAc/hexane) to provide 2.7 g of the desired product containing a small amount of the 3R diastereomer. ^{1}H NMR ($CDCl_3$): δ 2.57 (m, 1H), 2.70 (t, J=4.5 Hz, 1H), 2.90 - 3.05 (m, 1H), 4.20 (m, 1H), 4.70 (br d, 1H), 7.20-7.38 (m, 10H). Mass spectrum: $(M+H)^+$ = 298.

D. N(1)-Benzyloxycarbonyl-N(2)-benzyl hydrazine.

To a solution of 5 g of benzylhydrazine dihydrochloride in 50 ml of THF was added 5.9 ml of N-methylmorpholine and 7.6 g of CBz-NOS at 0°C. After 1 h, the reaction mixture was warmed to RT and stirred at RT overnight. After filtering off the solid formed and concentration of the filtrate; silica gel column chromatography (10% acetone/90% hexane) provided 2.6 g of desired product. ^{1}H NMR ($CDCl_3$): δ 3.25 (br s, 1H), 4.05 (s, 2H), 5.16 (s, 2H), 6.23 (br s, 1H), 7.25 (m, 10H).

E. 2-(Benzyloxycarbonyl)amino-4R-hydroxy-5R-(benzyloxycarbonyl)amino-1,6-diphenyl-2-azahexane.

To a solution of 1.2 g of the product of Example 1C in 36 ml of isopropanol was added 1.03 g of the hydrazine from Example 1D. The solution was heated at reflux for 24 h; cooled to RT and concentrated *in vacuo*. Silica gel column chromatography (10% to 20% acetone/hexane) provided 1.5 g of desired product. ^{1}H NMR ($CDCl_3$): δ 2.55 (m, 1H), 2.80 (m, 1H), 2.95 (d, 2H), 3.60 (m, 2H), 3.70 - 4.00 (m, 3H), 4.30 (s, 1H), 5.03 (s, 2H), 5.05 (s, 2H), 5.30 (m, 1H), 5.48 (s, 1H), 7.30 (m, 20H).

F. 2-(benzyloxycarbonyl)amino-4R-(trimethylsilyl-ethoxy-methoxy)-5R-(benzyloxycarbonyl)amino-1,6-diphenyl-2-azahexane.

To a solution of the product from Example 1E in 12 ml of dimethylformamide was added 1.8 ml of diisopropyl ethyl amine and then 1.14 ml of trimethylsilyl ethoxymethyl chloride. The reaction mixture was stirred at RT for 19 h. The DMF was removed *in vacuo*. The residue was extracted with EtOAc (3 x 80 ml) and washed with satd. NaCl solution. The organic layer was dried with anhy. sodium sulfate, filtered and the solvent evaporated *in vacuo*. Purification of the residue by silica gel column chromatography (20% acetone/hexane) provided 1.23 g (83%) of the desired compound. ^{1}H NMR ($CDCl_3$): δ 0.1 (s, 9H), 0.95 (t, 2H), 2.80 (m, 3H), 3.10 (m, 1H), 3.65 (m, 3H), 3.97 (m, 1H), 4.26 (m, 1H), 4.70 (m, 2H), 5.00 (m, 4H), 5.30 (m, 1H), 7.25 (m, 20H).

G. 2-Amino-4R-(trimethylsilyl-ethoxymethoxy)-5R-amino-1,6-diphenyl-2-azahexane.

To a suspension of 100 mg of 10% Pd/C in 20 ml of methanol was added 1.2 g of the product from Example 1F. The mixture was stirred vigorously under a hydrogen atmosphere (balloon filled with hydrogen) for 1 h. The catalyst was filtered off and the filtrate was concentrated *in vacuo* to provide 0.70 g of crude product. ^{1}H NMR ($CDCl_3$): δ 0.2 (s, 9H), 0.95 (t, 2H), 2.10 (m, 4H), 2.70 (m, 2H), 2.90 (m, 2H), 3.39 (m, 1H), 3.70 (m, 4H), 3.90 (m, 1H), 4.80 (m, 2H), 7.30 (m, 10H).

H. (5R,6R)-1,5-Dibenzyl-3-oxo-6-(trimethylsilylethoxy-methoxy)-1,2,4-triazacycloheptane.

To 120 ml of dichloromethane with stirring was added 300 mg of carbonyldiimidazole (in 5 ml of CH_2Cl_2) and 0.7 g of the product of Example 1G (in 5 ml of CH_2Cl_2) over a period of 2 h via a syringe pump. The solution was kept at RT for 72 h; concentration *in vacuo* and purification by silica gel column chromatography (20% EtOAc/CH_2Cl_2) provided 400 mg of desired compound. ^{1}H NMR ($CDCl_3$): δ 0.20 (s, 9H), 0.90 (t, 2H), 2.96 (m, 2H), 3.17 (m, 2H), 3.70 (m, 3H), 4.10 (m, 3H), 5.52 (br s, 1H), 4.75 (m, 2H), 5.70 (br s, 1H), 7.30 (m, 10H).

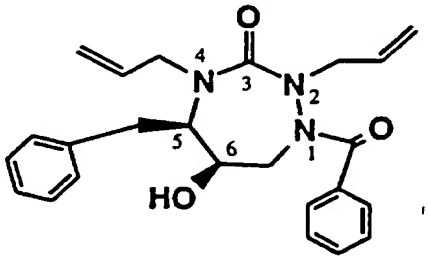
I. (5R,6R)-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

To a suspension of 72 mg of 20% palladium hydroxide on carbon in 36 ml of methanol was added 360 mg of the product of Example 1H. The mixture was stirred vigorously under a hydrogen atmosphere (balloon filled with hydrogen) for 1 h. The catalyst was filtered off and the filtrate was concentrated *in vacuo* to provide 285.0 mg of the desired product. ^{1}H NMR ($CDCl_3$) δ 0.01 (s, 9H), 0.92 (m, 2H), 2.92 (m, 3H), 3.33 (dd, 1H), 3.57-3.70 (m, 4H), 4.17 (br d, 1H), 4.32 (br s, 1H), 4.87 (dd, 2H), 5.95 (br s, 1H), 7.18-7.33 (m, 5H). Mass spectrum: $(M+H)^+$ = 352.

J. (5R,6R)-1-benzoyl-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

To a solution of 88 mg (0.25 mmol) of the product of Example 1I in 10 ml of CH_2Cl_2 was added 24.0 µl (0.30 mmol) of anhydrous pyridine and 32.0 µl (0.28 mmol) of benzoyl chloride. After being stirred at RT for 0.5 h, the mixture was treated with 2 ml of water, extracted with CH_2Cl_2 (4 X 5 ml). The combined organic solution was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography using 5% MeOH in CH_2Cl_2, provided 108.4 mg (95%) of desired product. Mass spectrum: $(M+H)^+$ = 456.

K. (5R,6R)-2,4-Bis-(2-propen-1-yl)-1-benzoyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.



To a suspension of 71 mg (2.4 mmol) of NaH (80% oil dispersion) in 0.5 ml of DMF was added a solution of 108.0 mg (0.24 mmol) of the product of Example 1J in 1.5 ml of DMF. After stirring at RT for 30 min, 123 µl (1.4 mmol) of allyl bromide was added. The reaction mixture was stirred at RT for 1h and quenched at 0°C with 5 ml of satd. NH_4Cl solution and extracted with CH_2Cl_2 (4 X 5 ml). The combined CH_2Cl_2 solution was washed with brine and dried. Concentration *in vacuo* and purification by silica gel column chromatography using 25% EtOAc in hexane, provided 110.4 mg of product. It was then deprotected by dissolving in 5 ml of MeOH, stirred with 125 µl of trimethylsilyl chloride at RT for 4 h. The reaction mixture was concentrated *in vacuo* and purified by silica gel column chromatography using 5% MeOH in CH_2Cl_2, provided 81.4 mg (85%) of desired product. Mass spectrum: $(M+H)^+$ = 406.

L. (5R,6R)-2,4-Bis-(1-propyl)-1-benzoyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

To a suspension of 25 mg of 10% Pd/C in 10 ml of EtOAc was added 50 mg of the product of Example 1K. The reaction mixture was stirred vigorously under a hydrogen atmosphere (hydrogen filled balloon) for 1.5 h. Filtration, concentration *in vacuo* and purification by silica gel column chromatography using 50% EtOAc in hexane provided 45.4 mg (90%) of desired product as a white foam. ^1H NMR ($CDCl_3$) δ 0.69-1.10 (six t, 6H), 1.24-1.45 (m, 2H), 1.55-2.01 (m, 2H), 2.42-2.93 (m, 1H), 3.00-3.28 (m, 3H), 3.33-3.54 (m, 2H), 3.60-3.72 (m, 2H), 3.92-4.13 (m, 2H), 4.26-4.86 (m, 1H), 7.17-7.55 (m, 10H). Mass spectrum: $(M+H)^+$ = 410.

Example 2

A. (5R,6R)-1-acetyl-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with the acetyl chloride, provided the desired compound. ^1H

NMR ($CDCl_3$) δ 0.04 (s, 9H), 0.95 (m, 2H), 2.19 (s, 3H), 2.79 (dd, 1H), 2.96 (m, 1H), 3.69 (m, 4H), 4.04 (m, 1H), 4.40 (br s, 1H), 4.70 (d, 1H), 4.83 (dd, 1H), 4.85 (d, 1H), 6.84 (s, 1H), 7.18-7.39 (m, 5H). Mass spectrum: $(M+H)^+$ = 394.

B. (5R,6R)-2,4-Bis-(2-propen-1-yl)-1-acetyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 2A , provided the desired compound. ^1H NMR ($CDCl_3$) δ 1.99 (s, 3H), 2.33 (d, 1H), 2.48 (dd, 1H), 2.80 (dd, 1H), 2.98 (dd, 1H), 3.15 (dd, 1H), 3.43 (dt, 1H), 3.73 (dd, 1H), 3.95 (m, 1H), 4.06 (ddt, 1H), 4.47 (dd, 1H), 4.69 (dd, 1H), 4.88 (d, 1H), 5.00 (d, 1H), 5.32 (d, 1H), 5.39 (d, 1H), 5.47 (m, 1H), 6.04 (m, 1H), 7.18-7.34 (m, 5H). Mass spectrum: $(M+H)^+$ = 344.

C. (5R,6R)-2,4-Bis-(1-propyl)-1-acetyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1L, but replacing the product of Example 1K with the product of Example 2B, provided the desired compound. ^1H NMR ($CDCl_3$) δ 0.68 (t, 3H), 1.02 (t, 3H), 1.21 (m, 2H), 1.77 (q, 2H), 1.91 (m, 1H), 2.00 (s, 3H), 2.86 (dd, 1H), 2.98-3.07 (m, 3H), 3.14 (dd, 1H), 3.39 (dt, 1H), 3.50 (m, 1H), 3.98 (m, 1H), 4.07 (m, 1H), 4.53 (dd, 1H), 7.19-7.32 (m, 5H). Mass spectrum: $(M+H)^+$ = 348.

Anal. Calcd. for $C_{19}H_{29}N_3O_3 \cdot 0.5H_2O$: C, 64.84; H, 8.45; N, 11.94; Found: C, 64.73; H, 8.23; N, 11.70.

Example 3

A. (5R,6R)-1-propionyl-5-benzyl-6-(trimethylsilyl-ethoxy-methoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with propionyl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 408.

B. (5R,6R)-2,4-Bis-(2-propen-1-yl)-1-propionyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product from Example 3A, provided the desired compound. Mass spectrum: $(M+H)^+ = 358$.

C. (5R,6R)-2,4-Bis-(1-propyl)-1-propionyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1L, but replacing the product of Example 1K with the product of Example 3B, provided the desired compound. ^1H NMR ($CDCl_3$) δ 0.66 (t, 3H), 1.03 (t, 3H), 1.08 (t, 3H), 1.14-1.27 (m, 2H), 1.76 (m, 2H), 1.82 (ddd, 1H), 2.23 (m, 1H), 2.33 (m, 2H), 2.86 (dd, 1H), 3.00 (m, 1H), 3.13 (dd, 2H), 3.37 (dt, 1H), 3.48 (dt, 1H). 3.96-4.03 (m, 1H), 4.06-4.12 (m, 1H), 4.54 (dd, 1H), 7.19-7.34 (m, 5H). Mass spectrum: $(M+H)^+ = 362$.

Anal. Calcd. for $C_{20}H_{31}N_3O_3$: C, 66.45; H, 8.64; N, 11.62; Found: C, 66.36; H, 8.61; N, 11.55.

Example 4

A. (5R,6R)-1-(2-methylpropionyl)-5-benzyl-6-(trimethyl-silylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with isobutyryl chloride, provided the desired compound. ^1H NMR ($CDCl_3$) δ 0.03 (s, 9H), 0.96 (t, 2H), 1.12 (d, 6H), 2.79 (m, 1H), 2.94 (m, 1H), 3.11 (m, 1H), 3.21 (m, 1H), 3.70 (m, 3H), 4.08 (m, 1H), 4.41 (br s, 1H), 4.71 (d, 1H), 4.77 (m, 1H), 4.85 (d, 1H), 6.74 (br s, 1H), 7.18 (m, 2H), 7.25-7.35 (m, 3H). Mass spectrum: $(M+H)^+ = 422$.

B. (5R,6R)-2,4-Bis-(2-propen-1-yl)-1-(2-methylpropionyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 4A, provided the desired compound.

C. (5R,6R)-2,4-Bis-(1-propyl)-1-(2-methylpropionyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1L, but replacing the product of Example 1K with the product of Example 4B , provided the desired compound. ^{1}H NMR ($CDCl_3$) δ 0.65 (t, 3H), 0.99 (d, 3H), 1.03 (t, 3H), 1.14 (d, 3H),1.22 (m, 2H), 1.78 (m, 2H), 1.91 (m, 1H), 2.74 (m, 1H), 2.88 (dd, 1H), 3.03 (m, 3H), 3.15 (m, 1H), 3.41 (m, 1H), 3.92 (m, 1H), 4.06 (ddd, 1H), 4.58 (dd, 1H), 7.19-7.33 (m, 5H). Mass spectrum: $(M+H)^+$ = 376.

Anal. Calcd. for $C_{21}H_{33}N_3O_3$: C, 67.17; H, 8.86; N, 11.19; Found: C, 67.29; H, 9.14; N, 11.15.

Example 5

A. (5R,6R)-1-(2,2-dimethylpropionyl)-5-benzyl-6-(trimethyl-silylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with pivaloyl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 436.

B. (5R,6R)-2,4-Bis-(2-propen-1-yl)-1-(2,2-dimethylpropionyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 5A, provided the desired compound.

C. (5R,6R)-2,4-Bis-(1-propyl)-1-(2,2-dimethyl-propionyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1L, but replacing the product of Example 1K with the product of Example 5B, provided the desired compound. Mass spectrum: $(M+H)^+$ = 390.

Anal. Calcd. for $C_{22}H_{35}N_3O_3$: C, 67.83; H, 9.06; N, 10.79; Found: C, 67.73; H, 9.19; N, 10.66.

Example 6

A. (5R,6R)-1-methanesulfonyl-5-benzyl-6-(trimethyl-silyl-ethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

To a solution of 100 mg (0.28 mmol) of the product of Example 1I in 5 ml of CH_2Cl_2 was added 95.2 µl (0.68 mmol) of triethylamine and 48.4 µl (0.64 mmol) of methanesulfonyl chloride. The mixture was stirred at 0°C for 2 h and then at RT for 5 h. Evaporated the solvent. The residue was purified by silica gel column chromatography using 70% EtOAc in hexane, provided 68.6 mg (57%) of desired product. ^1H NMR ($CDCl_3$) δ 0.04 (s, 9H), 0.97 (m, 2H), 2.89 (dd, 1H), 3.00 (dd, 1H), 3.14 (s, 3H), 3.36 (br d, 1H), 3.64-3.85 (m, 4H), 4.35 (br d, 1H), 4.38 (br s, 1H), 4.74 (d, 1H), 4.88 (d, 1H), 6.57 (d, 1H), 7.20-7.28 (m, 5H). Mass spectrum: $(M+H)^+$ = 430.

B. (5R,6R)-2,4-Bis-(2-propen-1-yl)-1-methane-sulfonyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product from Example 1J with the product from Example 6A, provided the desired compound. ^1H NMR ($CDCl_3$) 1.93 (d, 1H), 2.58 (dd, 1H), 2.88 (dd, 1H), 3.00 (s, 3H), 3.09 (dd, 1H), 3.25 (dd, 1H), 3.47 (dt, 1H), 3.96 (m, 2H), 4.14 (m, 2H), 4.58 (dd, 1H), 4.94 (d, 1H), 5.03 (d, 1H), 5.33 (d,

1H), 5.39 (d, 1H), 5.56 (m, 1H), 6.04 (m, 1H), 7.15-7.32 (m, 5H). Mass spectrum: $(M+H)^+$ = 380.

Anal. Calcd. for $C_{18}H_{25}N_3O_4S$: C, 56.97; H, 6.64; N, 11.07; Found: C, 56.93; H, 6.73; N, 10.94.

Example 7

A. (5R,6R)-1-bromoacetyl-5-benzyl-6-(trimethylsilyl-ethoxy-methoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with the bromoacetyl chloride, provided the desired compound. ^1H NMR ($CDCl_3$) δ 0.03 (s, 9H), 0.95 (m, 2H), 2.79 (dd, 1H), 2.94 (m, 1H), 3.73 (m, 4H), 4.06 (m, 1H), 4.23 (br s, 2H), 4.49 (br s, 1H), 4.71 (m, 2H), 4.86 (br d, 1H), 7.18-7.39 (m, 6H). Mass spectrum: $(M+NH_4)^+$ = 491, 489.

B. (5R,6R)-1-(N,N-dimethylglycyl)-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

To a solution of 60 mg (0.13 mmol) of the product of Example 7A in 3 ml of CH_2Cl_2 was added 0.5 ml (0.64 mmol) of 1.3 M dimethylamine in ether. The mixture was stirred at RT for 2 h and then treated with 3 ml of water, extracted with CH_2Cl_2 (4 X 5 ml). The combined organic solution was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography using 10% MeOH in CH_2Cl_2, provided 55.4 mg (100%) of desired product. ^1H NMR ($CDCl_3$) δ 0.03 (s, 9H), 0.97 (m, 2H), 2.32 (s, 6H), 2.88 (dd, 1H), 3.00 (dd, 1H), 3.09 (m, 1H), 3.27 (m, 1H), 3.67 (m, 2H), 3.79 (m, 2H), 3.92 (br s, 1H), 4.14 (br s, 1H), 4.40 (br s, 1H), 4.73 (d, 1H), 4.91 (d, 1H), 7.19-7.37 (m, 5H), 8.94 (br s, 1H). Mass spectrum: $(M+H)^+$ = 437.

C. (5R,6R)-2,4-Bis-cyclopropylmethyl-1-(N,N-dimethylglycyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1L, but replacing the product from Example 1K with the product of Example 7B and replacing the allyl bromide with bromomethyl cyclopropane, provided the desired compound. ^{1}H NMR ($CDCl_3$) δ 0.36 (m, 4H), 0.67 (m, 4H), 1.12 (m, 1H), 1.87 (dd, 1H), 2.32 (s, 6H), 2.86 (dd, 1H), 2.91-3.34 (m, 8H), 3.57 (m, 1H), 3.79 (m, 1H), 3.95 (dd, 1H), 4.07 (m, 1H), 4.55 (dd, 1H), 7.20-7.33 (m, 5H). Mass spectrum: $(M+H)^+$ = 415.

Example 8

A. (5R,6R)-1-(2-furoyl)-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with 2-furoyl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 446.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(2-furoyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 8A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 528.

Anal. Calcd. for $C_{30}H_{29}N_3O_6 \cdot 0.5H_2O$: C, 67.15; H, 5.64; N, 7.83; Found: C, 66.99; H, 5.49; N, 7.74.

Example 9

(5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-acetyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 2A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride,

provided the desired compound. ^{1}H NMR (DMSO-D_6) (mixture of three rotamers) δ 1.83, 1.87 and 2.03 (three s, 3H), 2.33-2.45 (m, 1H), 2.60 (m, 1H), 2.73 (m, 1H), 2.83 (m, 1H), 3.13-3.23 (m, 1H), 3.55-3.68 (m, 1H), 3.95, 4.17 and 4.25 (three d, 1H), 4.28, 4.36 and 4.55 (three d, 1H), 4.89, 4.92 and 4.96 (three d, 1H), 5.36, 5.38 and 5.48 (three d, 1H), 6.63 (m, 4H), 6.78 (m, 2H), 7.02 (m, 2H), 7.17-7.34 (m, 5H), 9.29, 9.34, 9.35, 9.39, 9.47 and 9.52 (six s, 2H). Mass spectrum: $(M+H)^+$ = 528.

Anal. Calcd. for $C_{27}H_{29}N_3O_5 \cdot 0.75H_2O$: C, 66.31; H, 6.29; N, 8.59; Found: C, 66.35; H, 6.16; N, 8.59.

Example 10

(5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(2-methyl-propionyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 4A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^{1}H NMR (DMSO-d_6) (mixture of three rotamers) 0.86-1.09 (six d, 3H), 2.33-2.46, (m, 1H), 2.66-3.03 (m, 4H), 3.24 (m, 1H), 3.42-3.78 (three m, 1H), 3.98-4.08 (m, 1H), 4.28, 4.46 and 4.60 (three d, 1H), 4.81, 4.83 and 5.03 (three d, 1H), 5.12, 5.16 and 5.28 (three d, 1H), 6.60-6.80 (m, 6H), 6.98-7.33 (m, 7H), 9.03-9.23 (six s, 2H). Mass spectrum: $(M+H)^+$ = 521.

Anal. Calcd. for $C_{29}H_{33}N_3O_5 \cdot 0.5H_2O$: C, 67.95; H, 6.69; N, 8.20; Found: C, 67.87; H, 6.60; N, 8.11.

Example 11

A. (5R,6R)-1-(butyryl)-5-benzyl-6-(trimethylsilyl-ethoxy-methoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with butyryl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 422.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(butyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 11A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^{1}H NMR (DMSO-d$_6$) (mixture of three rotamers) 0.81 and 0.94 (three t, 3H), 1.44-1.57, (m, 2H), 2.34-2.67 (m, 1H), 2.73-2.97 (m, 2H), 3.22 (m, 1H), 3.63-3.72 (m, 1H), 3.98 (m, 1H), 4.12-4.23 (m, 1H), 4.22-4.56 (three d, 1H), 4.85-4.98 (three d, 1H), 5.33-5.47 (three d, 1H), 6.60-6.79 (m, 6H), 6.98-7.35 (m, 7H), 9.33 (br s, 1H), 9.46 (br s, 1H). Mass spectrum: $(M+H)^+$ = 504.

Example 12

A. (5R,6R)-1-(3-methylbutyryl)-5-benzyl-6-(trimethylsilyl-ethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with isovaleryl chloride, provided the desired compound. ^{1}H NMR ($CDCl_3$) δ 0.03 (s, 9H), 0.96 (m, 8H), 2.15 (m, 1H), 2.36 (m, 2H), 2.77 (m, 1H), 2.95 (m, 1H), 3.71 (m, 3H), 4.06 (m, 1H), 4.36 (br s, 1H), 4.72 (d, 1H), 4.81 (m, 1H), 4.87 (d, 1H), 6.50 (br s, 1H), 7.16-7.35 (m, 5H). Mass spectrum: $(M+H)^+$ = 436.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 12A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^{1}H NMR (DMSO-d$_6$) (mixture of three rotamers) 0.81-0.95 (four d, 6H), 1.72-2.45 (m, 4H), 2.56-2.86 (m, 1H), 3.03-3.25 (m, 1H), 3.63 (m, 1H), 4.18 (m, 1H), 4.25, 4.38 and 4.53 (three d, 1H), 4.94 (m, 1H), 5.33, 5.38 and 5.46 (three d, 1H), 6.61-

6.79 (m, 6H), 6.98-7.32 (m, 7H), 9.33, 9.39 and 9.47 (three br s, 2H). Mass spectrum: $(M+H)^+$ = 518.

Example 13

A. (5R,6R)-1-valeryl-5-benzyl-6-(trimethylsilyl-ethoxy-methoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with valeryl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 436.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-valeryl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 13A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^1H NMR (DMSO-D_6) (mixture of three rotamers) δ 0.81, 0.87 and 0.92 (three t, 3H), 1.19, 1.37 and 1.52 (three m, 4H), 1.90, 2.13 and 1.32 (three m, 2H), 2.39 (m, 1H), 2.62-2.97 (m, 3H), 3.07-3.22 (m, 1H), 3.60-3.65 (m, 1H), 3.92, 3.96 and 4.03 (three d, 1H), 3.97, 4.16 and 4.21 (three d, 1H), 4.29, 4.38 and 4.52 (three d, 1H), 4.83, 4.89 and 4.95 (three d, 1H), 5.35, 5.38 and 5.47 (three d, 1H), 6.61 (m, 4H), 6.76 (m, 2H), 7.03(m, 2H), 7.16-7.33 (m, 5H), 9.30, 9.35, 9.39 and 9.47 (four br s, 2H). Mass spectrum: $(M+H)^+$ = 518.

Anal. Calcd. for $C_{30}H_{35}N_3O_5 \cdot 0.5H_2O$: C, 68.42; H, 6.89; N, 7.98; Found: C, 68.54; H, 6.79; N, 7.72.

Example 14

A. (5R,6R)-1-(2-ethylbutyryl)-5-benzyl-6-(trimethylsilyl-ethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with 2-ethylbutyryl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 450.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(2-ethylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 14A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^1H NMR (DMSO-D_6) (mixtures of three rotamers) δ 0.75-0.96 (three m, 6H), 1.25-1.58 (three m, 4H), 2.36-2.46 (m, 1H), 2.65-2.85 (m, 3H), 3.15-3.25 (m, 2H), 3.68 (m, 1H), 3.95 (d, 1H), 4.10 (m, 1H), 4.38 (d, 1H), 4.95, 5.06 and 5.13 (three d, 1H), 5.38, 5.40 and 5.44 (three d, 1H), 6.57-6.63 (m, 4H), 6.87 (dd, 2H), 6.90 (dd, 1H), 7.12 (dd, 1H), 7.22-7.32 (m, 5H), 9.28, 9.32, 9.38, 9.40, 9.48 and 9.51 (six s, 2H). Mass spectrum: $(M+NH_4)^+$ = 549.

Anal. Calcd. for $C_{31}H_{37}N_3O_5 \cdot 0.5H_2O$: C, 68.87; H, 7.08; N, 7.77; Found: C, 68.88; H, 7.09; N, 7.68.

Example 15

A. (5R,6R)-1-(2-(1-propylvaleryl))-5-benzyl-6-(trimethylsilyl-ethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with 2-(1-propylvaleryl) chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 478.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(2-(1-propylvaleryl))-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 15A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^{1}H NMR (DMSO-D$_6$) (mixtures of three rotamers) δ 0.72, 0.85 and 0.87 (three t, 6H), 1.18-1.57 (m, 8H), 2.28-2.38 (m, 1H), 2.58-3.18 (m, 5H), 3.67 (dd, 1H), 3.97 (d, 1H), 4.03, 4.07 and 4.11 (three d, 1H), 4.12, 4.37 and 4.58 (three d, 1H), 4.94, 5.08 and 5.15 (three d, 1H), 5.35, 5.40 and 5.42 (three d, 1H), 6.52-6.63 (m, 4H), 6.74-6.79 (m, 2H), 6.87 (m, 1H), 7.09-7.16(m, 2H), 7.23-7.36 (m, 4H), 9.26, 9.31, 9.36, 9.37, 9.46 and 9.48 (six s, 2H). Mass spectrum: $(M+NH_4)^+$ = 577.

Anal. Calcd. for $C_{33}H_{41}N_3O_5 \cdot 0.5H_2O$: C, 69.69; H, 7.44; N, 7.39; Found: C, 69.95; H, 7.37; N, 7.31.

Example 16

A. (5R,6R)-1-cyclopentanecarbonyl-5-benzyl-6-(trimethyl-silylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with cyclopentanecarbonyl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 448.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-cyclopentane-carbonyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 16A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^{1}H NMR (DMSO-D$_6$) (mixtures of three rotamers) δ 1.94-1.85 (m, 8H), 2.23-2.30 (m, 1H), 2.61-3.18 (m, 5H), 3.66 (d, 1H), 3.98, 4.01 and 4.03 (three d, 1H), 4.08, 4.17 and

4.22 (three d, 1H), 4.30, 4.42 and 4.57 (three d, 1H), 4.82, 4.84 and 5.01 (three d, 1H), 5.31, 5.35 and 5.46 (three d, 1H), 6.58-6.66 (m, 4H), 6.73-6.79 (m, 2H), 6.97-6.99 (m, 1H), 7.09-7.15 (m, 2H), 7.19-7.34 (m, 4H), 9.29, 9.34, 9.37 and 9.45 (four br s, 2H). Mass spectrum: $(M+NH_4)^+ = 547$.

Anal. Calcd. for $C_{31}H_{35}N_3O_5 \cdot 0.75H_2O$: C, 68.55; H, 6.77; N, 7.74; Found: C, 68.51; H, 6.47; N, 7.52.

Example 17

(5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(N,N-dimethylglycyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 7B and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^1H NMR (DMSO-d_6) (mixture of three rotamers) 2.17 (s, 3H), 2.22, (s, 3H), 2.27-2.44 (m, 1H), 2.55-3.03 (m, 5H), 3.18 (m, 1H), 3.78-4.00 (m, 2H), 4.23 (m, 1H), 4.33-4.41 (m, 1H), 4.92 (m, 1H), 5.32, 5.39 and 5.50 (three d, 1H), 6.57-6.66 (m, 4H), 6.76 (m, 2H), 7.03 (m, 2H), 7.17-7.32 (m, 5H), 9.28-9.52 (six s, 2H). Mass spectrum: $(M+H)^+ = 519$.

Example 18

A. (5R,6R)-1-(4-morpholinylacetyl)-5-benzyl-6-(trimethyl-silylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 7B, but replacing the dimethylamine with morpholine, provided the desired compound. Mass spectrum: $(M+NH_4)^+ = 479$.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(4-morpholinylacetyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 18A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^{1}H NMR (DMSO-d_6) (mixture of three rotamers) 2.37-2.47 (m, 5H), 2.63-3.14 (m, 5H), 3.24 (m, 1H), 3.47-3.59 (m, 2H), 3.82 (m, 1H), 4.00 (m, 1H), 4.25 (m, 1H), 4.34-4.43 (m, 1H), 4.91 (m, 1H), 5.32, 5.40, 5.47 (three d, 1H), 6.58-6.77 (m, 6H), 7.01-7.34 (m, 7H), 9.29-9.51 (six s, 2H). Mass spectrum: $(M+H)^+$ = 561.

Anal. Calcd. for $C_{31}H_{36}N_4O_6 \cdot 0.75H_2O$: C, 64.85; H, 6.58; N, 9.76; Found: C, 64.58; H, 6.47; N, 9.61.

Example 19

A. (5R,6R)-1-methoxyacetyl-5-benzyl-6-(trimethylsilyl-ethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with methoxyacetyl chloride, provided the desired compound. ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 9H), 0.95 (m, 2H), 2.80 (dd, 1H), 2.96 (dd, 1H), 3.45 (s, 3H), 3.66-3.76 (m, 3H), 4.03 (m, 1H), 4.20 (dd, 2H), 4.41 (s, 1H), 4.72 (d, 1H), 4.88 (d, 1H), 6.95 (br s, 1H), 7.18-7.36 (m, 5H). Mass spectrum: $(M+H)^+$ = 441.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-methoxyacetyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 19A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 523.

Anal. Calcd. for $C_{28}H_{31}N_3O_6 \cdot 0.75H_2O$: C, 64.79; H, 6.31; N, 8.09; Found: C, 64.99; H, 6.16; N, 8.00.

Example 20

A. (5R,6R)-1-(t-butoxycarbonyl)-5-benzyl-6-(trimethyl-silylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

To a solution of 50 mg (0.14 mmol) of the product of Example 1I in 3 ml of CH_2Cl_2 was added 46.6 mg of di-*tert*-butyl dicarbonate, 4 mg of DMAP and 40 µl of triethylamine. The mixture was stirred at RT for 20 h and then treated with 3 ml of water, extracted with CH_2Cl_2 (5 X 5 ml). The combined organic solution was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography using 50% EtOAc in hexane, provided 53.7 mg (84%) of desired product. Mass spectrum: $(M+H)^+$ = 452.

B. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(t-butoxycarbonyl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 20A and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. Mass spectrum: $(M+H)^+$ = 534.

Example 21

A. (5R,6R)-1-(4-methoxycarbonylbutyryl)-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1J, but replacing the benzoyl chloride with methyl glutaryl chloride, provided the desired compound. Mass spectrum: $(M+NH)^+$ = 480.

B. (5R,6R)-1-(5-hydroxyvaleryl)-5-benzyl-6-(trimethyl-silylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

To a solution of 261.3 mg (0.54 mmol) of the product of Example 21A in 30 ml of THF was added 1.6 ml of $LiBH_4$ (2.0 M in THF). The mixture was stirred at RT for 20 h. It was then treated with 10 ml of 10% citric acid solution at 0°C and extracted with CH_2Cl_2 (5 x 20 ml). The combined organic solution was dried over Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography using 5% MeOH in CH_2Cl_2, provided 164.5 mg (67%) of desired product. Mass spectrum: $(M+NH)^+$ = 452.

C. (5R,6R)-1-(5-trimethylsilylethoxymethoxy-valeryl)-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of 1F, but replacing the product of Example 1E with the product of Example 21B, provided the desired compound. Mass spectrum: $(M+NH)^+$ = 582.

D. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(5-hydroxyvaleryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 21C and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^1H NMR (DMSO-D_6) (mixtures of three rotamers) δ 1.34-1.61 (m, 4H), 2.07-2.47 (m, 2H), 2.55-2.96 (m, 3H), 3.16-3.24 (m, 3H), 3.38-3.46 (m, 1H), 3.60-3.65 (m, 1H), 3.94-4.02 (m, 1H), 4.09, 4.10 and 4.12 (three d, 1H), 4.15, 4.23 and 4.25 (three d, 1H), 4.37, 4.40 and 4.46 (three t, 1H), 4.54, 4.90 and 4.97 (three d, 1H), 5.34, 5.37 and 5.46 (three d, 1H), 6.60-6.62 (m, 4H), 6.75-6.78 (m, 2H), 6.98-7.10 (m, 2H), 7.17-7.32 (m, 5H), 9.28, 9.32, 9.34, 9.38, 9.46 and 9.49 (six s, 2H). Mass spectrum: $(M+H)^+$ = 534.

Anal. Calcd. for $C_{30}H_{35}N_3O_6 \cdot H_2O$: C, 65.32; H, 6.76; N, 7.62; Found: C, 65.46; H, 6.62; N, 7.46.

Example 22

A. (5R,6R)-1-(3-ethoxycarbonylpropionyl)-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of 1J, but replacing the benzoyl chloride with ethyl succinyl chloride, provided the desired compound. Mass spectrum: $(M+NH)^+ = 480$.

B. (5R,6R)-1-(4-hydroxybutyryl)-5-benzyl-6-(trimethyl-silylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of 21A, but replacing the product of Example 21A with the product of Example 22A, provided the desired compound. Mass spectrum: $(M+NH)^+ = 438$.

C. (5R,6R)-1-(4-trimethylsilylethoxymethoxy-butyryl)-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1F, but replacing the product of Example 1E with the product of Example 22B, provided the desired compound. Mass spectrum: $(M+NH)^+ = 568$.

D. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(4-hydroxybutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 22C and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^1H NMR (DMSO-D_6) (mixture of three rotamers) δ 1.57-1.75 (m, 2H), 2.32-2.47 (m, 2H), 2.56-2.90 (m, 3H), 3.15-3.22 (m, 3H), 3.42-3.47 (m, 1H), 3.63 (m, 1H), 3.97 (m, 1H),

4.08, 4.10 and 4.13 (three d, 1H), 4.15, 4.24 and 4.38 (three d, 1H), 4.48, 4.54 and 4.56 (three t, 2H), 4.89 4.93 and 5.02 (three d, 1H), 5.36, 5.38 and 5.44 (three d, 1H), 6.61 (m, 4H), 6.76-6.79 (m, 2H), 7.02-7.06 (m, 2H), 7.18-7.31 (m, 5H), 9.28, 9.33,9.34, 9.39, 9.47 and 9.49 (six s, 2H). Mass spectrum: $(M+H)^+$ = 520.

Anal. Calcd. for $C_{29}H_{33}N_3O_6 \cdot H_2O$: C, 64.79; H, 6.56; N, 7.82; Found: C, 64.83; H, 6.38; N, 7.72.

Example 23

A. (5R,6R)-1-(benzyloxyacetyl)-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of 1J, but replacing the benzoyl chloride with benzyloxyacetyl chloride, provided the desired compound. Mass spectrum: $(M+NH)^+$ = 500.

B. (5R,6R)-1-(hydroxyacetyl)-5-benzyl-6-(trimethylsilylethoxy-methoxy)-3-oxo-1,2,4-triazacycloheptane.

To a suspension of 150 mg of 10% palladium on carbon in 10 ml of ethanol (95%) was added 143.8 mg of the product of Example 23A. The mixture was stirred vigorously under a hydrogen atmosphere (balloon filled with hydrogen) for 2 days. The catalyst was filtered off and the filtrate was concentrated *in vacuo* to provide 103.2 mg of the desired product. Mass spectrum: $(M+NH_4)^+$ = 427.

C. (5R,6R)-1-(trimethylsilylethoxymethoxyacetyl)-5-benzyl-6-(trimethylsilylethoxymethoxy)-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1F, but replacing the product of 1E with the product of Example 23B, provided the desired compound. Mass spectrum: $(M+NH)^+$ = 540.

D. (5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-hydroxyacetyl-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 23C and replacing the allyl bromide with 4-(2-trimethylsilylethoxymethoxy)benzyl chloride, provided the desired compound. ^{1}H NMR (DMSO-D$_6$) (mixture of three rotamers) δ 2.58-2.79 (m, 3H), 3.10-3.25 (m, 2H), 3.39-3.48 (m, 1H), 3.65 (m, 1H), 3.87 (m, 1H), 4.08 (d, 1H), 4.33, 4.39 and 4.46 (three d, 2H), 4.80, 4.94 and 4.95 (three d, 1H), 5.43, 5.46 and 5.61 (three d, 1H), 6.64-6.76 (m, 6H), 7.03-7.33 (m, 7H), 7.73, 7.98 and 8.12 (three s, 1H), 9.30,9.33, 9.35, 9.43, 9.47 and 9.50 (six s, 2H). Mass spectrum: $(M+NH_4)^+$ = 509.

Example 24

(5R,6R)-2,4-Bis-(3-nitrobenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 12A and replacing the allyl bromide with 3-nitrobenzyl bromide, provided the desired compound. ^{1}H NMR (DMSO-d6) (mixture of three rotamers) 0.65-0.94 (six d, 6H), 1.54-2.37 (m, 4H), 2.64-3.22 (m, 3H), 3.32-4.18 (m, 3H), 4.26-4.32 (m, 1H), 4.48-4.60 (m, 1H), 5.14, 5.17 and 5.18 (three d, 1H), 5.46, 5.50 and 5.51 (three d, 1H), 6.86-8.41 (m, 13H). Mass spectrum: $(M+H)^+$ =576.

Anal. Calcd. for $C_{30}H_{33}N_5O_7 \cdot 0.5H_2O$: C, 61.63; H, 5.86; N, 11.98; Found: C, 61.70; H, 5.65; N, 11.72.

Example 25

(5R,6R)-2,4-Bis-(3-aminobenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

To a suspension of 150 mg of Raney-Ni (50% in water) in 15 ml of MeOH/THF (1:1) was added 150 mg of the product of Example 24.

The reaction mixture was stirred vigorously under a hydrogen atmosphere (hydrogen filled balloon) for 2 h. Filtration, concentration *in vacuo* and purification by silica gel column chromatography using 5% MeOH in CH_2Cl_2 provided 119.0 mg (89%) of desired product as a white foam. ^1H NMR (DMSO-d_6) (mixture of three rotamers) 0.84-0.97 (six d, 6H), 1.82-2.63, (m, 4H), 2.80-4.04 (m, 6H), 3.92, 4.06 and 4.13 (three d, 1H), 4.24, 4.39 and 4.52 (three d, 1H), 4.87-5.11 (m, 5H), 5.30, 5.32 and 5.38 (three d, 1H), 5.95-6.03 (m, 2H), 6.37-7.32 (m, 11H). Mass spectrum: $(M+H)^+$ = 516.

Anal. Calcd. for $C_{30}H_{37}N_5O_3 \cdot 0.25H_2O$: C, 69.27; H, 7.27; N, 13.46; Found: C, 69.34; H, 7.21; N, 13.34.

Example 26

(5R,6R)-2,4-Bis-(4-nitrobenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 1K, but replacing the product of Example 1J with the product of Example 12A and replacing the allyl bromide with 4-nitrobenzyl bromide, provided the desired compound. ^1H NMR (DMSO-d_6) (mixture of two rotamers) 0.68-0.94 (four d, 6H), 1.57-2.38, (m, 4H), 2.63-3.20 (m, 3H), 3.31-4.16 (m, 3H), 4.25 and 4.31 (two d, 1H), 4.49 and 4.57 (two dd, 1H), 5.15 and 5.16 (two d, 1H), 5.44 and 5.49 (two d, 1H), 6.86-8.32 (m, 13H). Mass spectrum: $(M+H)^+$ =576.

Anal. Calcd. for $C_{30}H_{33}N_5O_7 \cdot 0.5H_2O$: C, 61.63; H, 5.86; N, 11.98; Found: C, 61.70; H, 5.65; N, 11.72.

Example 27

(5R,6R)-2,4-Bis-(4-aminobenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane.

Using the procedure of Example 25, but replacing the product of Example 24 with the product of Example 26, provided the desired compound. ^1H NMR (DMSO-d_6) (mixture of three rotamers) 0.85-0.99 (four d, 6H), 1.81-2.58, (m, 4H), 2.63-3.98 (m, 6H), 3.90, 4.04 and

4.12 (three d, 1H), 4.18, 4.32 and 4.51 (three d, 1H), 4.81-5,09 (m, 5H), 5.28, 5.31 and 5.40 (three d, 1H), 6.38-6.56 (m, 6H), 6.98-7.31 (m, 7H). Mass spectrum: $(M+H)^+$ =516.

Anal. Calcd. for $C_{30}H_{37}N_5O_3 \cdot 0.5H_2O$: C, 68.68; H, 7.30; N, 13.35; Found: C, 68.80; H, 7.15; N, 13.17.

Using the methods described above, the compounds shown in Tables 1-128 can be prepared. In the tables, Ph represents phenyl.

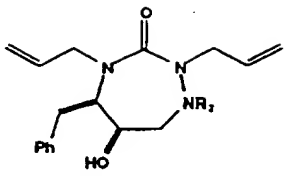


TABLE 1

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl

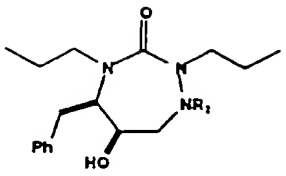


TABLE 2

R_2
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

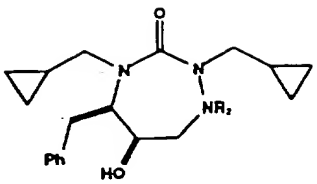


TABLE 3

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

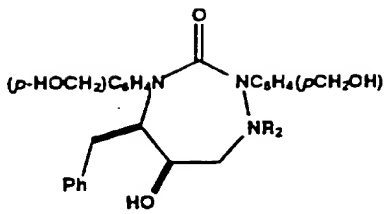


TABLE 4

R_2
benzoyl
propionyl
2,2-dimethylpropionyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
3-hydroxypropionyl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
3-furoyl
methanesulfonyl

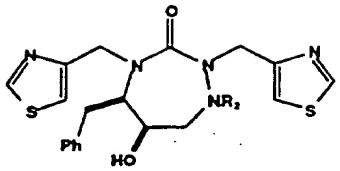


TABLE 5

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

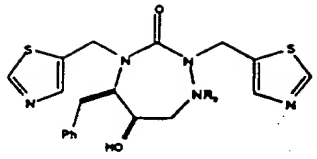


TABLE 6

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

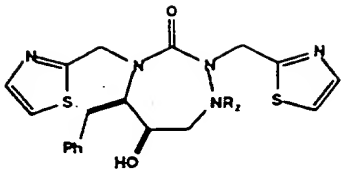


TABLE 7

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furcyl
3-furoyl
methanesulfonyl

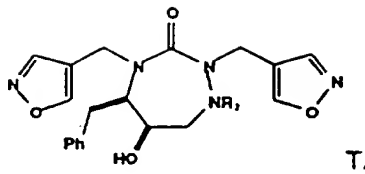


TABLE 8

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

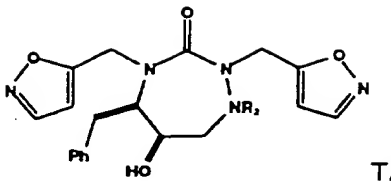


TABLE 9

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

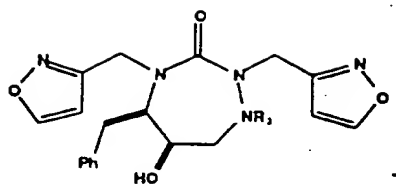


TABLE 10

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
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methanesulfonyl

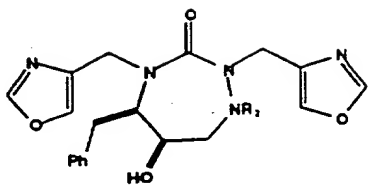

TABLE 11

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

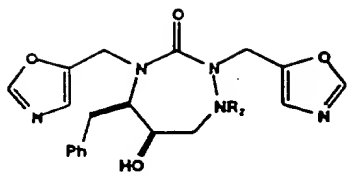

TABLE 12

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

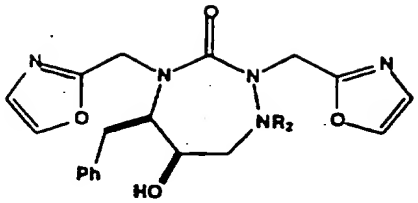

TABLE 13

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

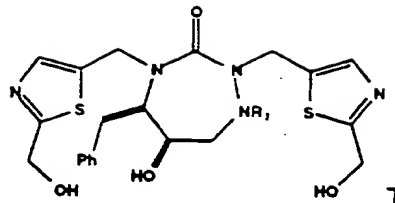

TABLE 14

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

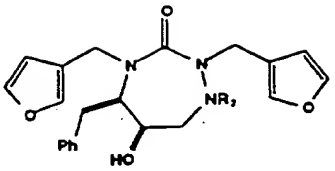

TABLE 15

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

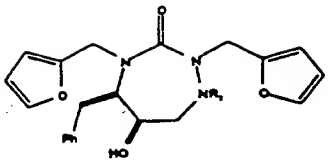

TABLE 16

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

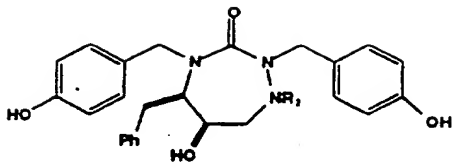

TABLE 17

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

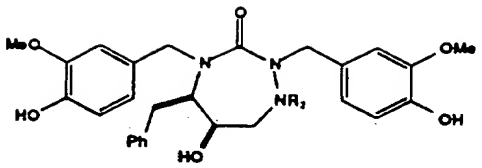

TABLE 18

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

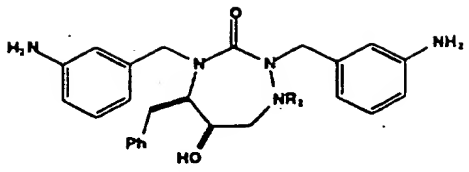

TABLE 19

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

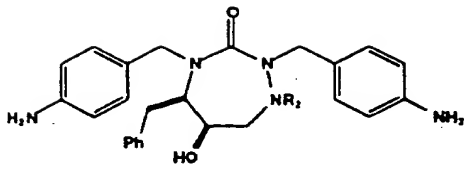

TABLE 20

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

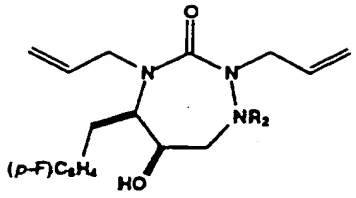

TABLE 21

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

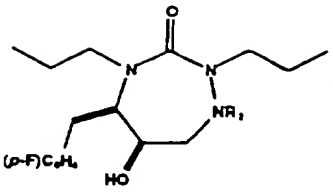

TABLE 22

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

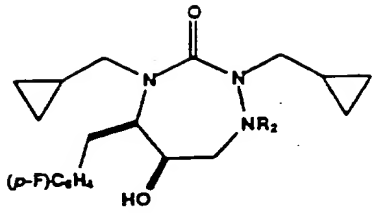

TABLE 23

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

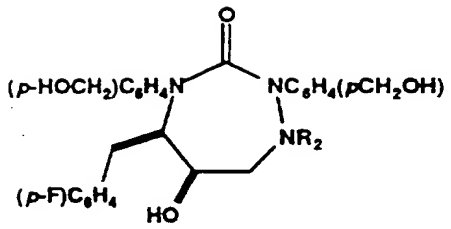

TABLE 24

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

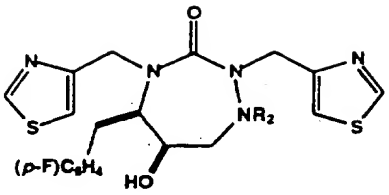

TABLE 25

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

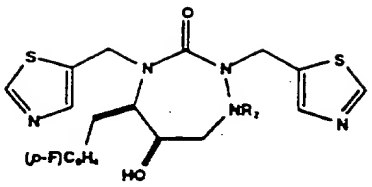

TABLE 26

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

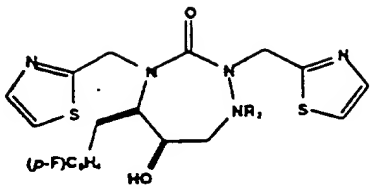

TABLE 27

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

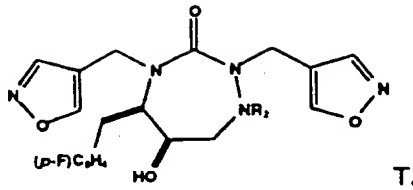

TABLE 28

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

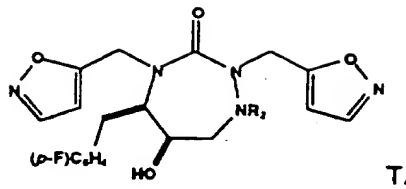

TABLE 29

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

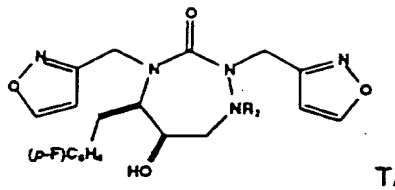

TABLE 30

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

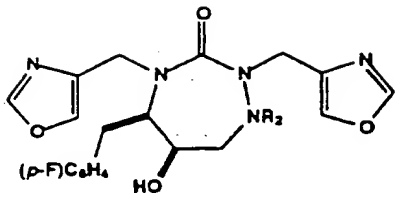

TABLE 31

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

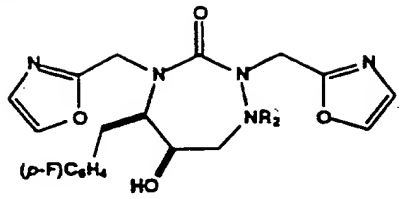

TABLE 32

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

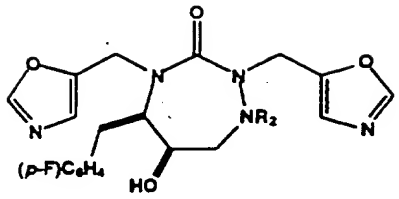

TABLE 33

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

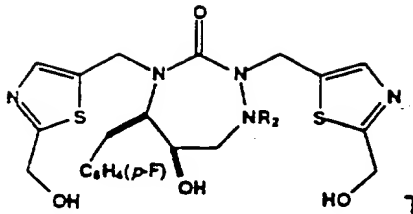

TABLE 34

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

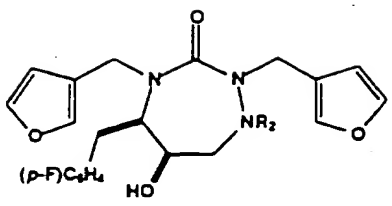

TABLE 35

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

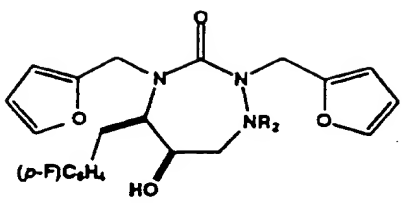

TABLE 36

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

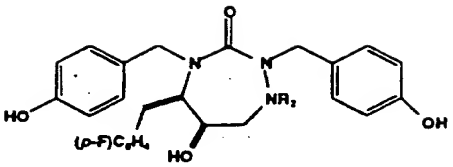

TABLE 37

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

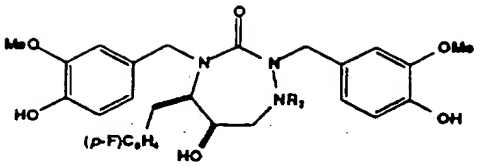

TABLE 38

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

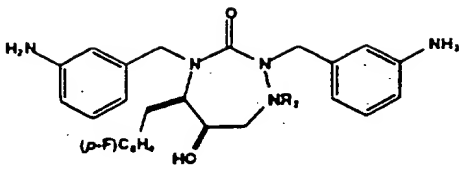

TABLE 39

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

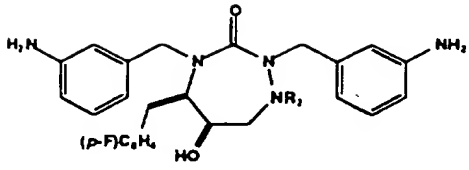

TABLE 40

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

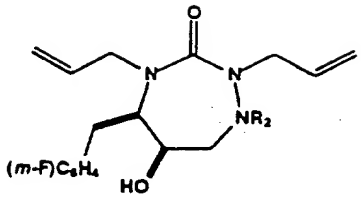

TABLE 41

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

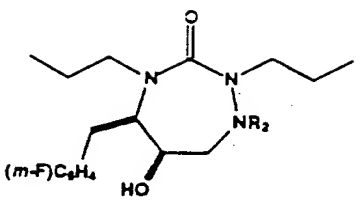

TABLE 42

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

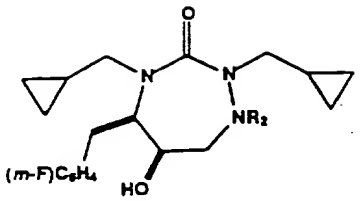

TABLE 43

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

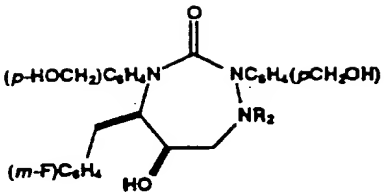

TABLE 44

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

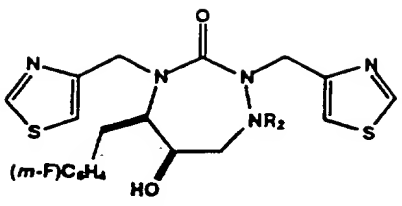

TABLE 45

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

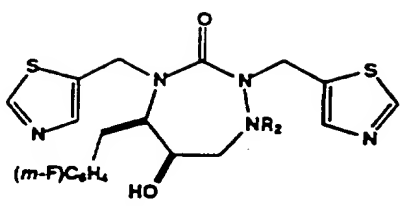

TABLE 46

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

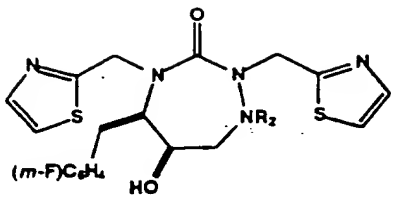

TABLE 47

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

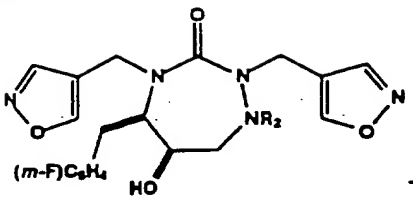

TABLE 48

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

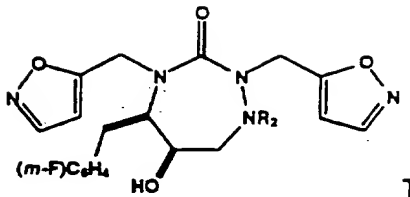

TABLE 49

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

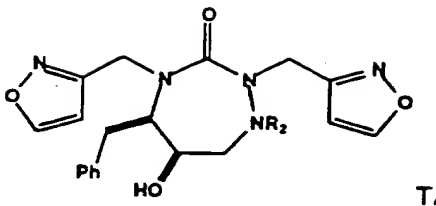

TABLE 50

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

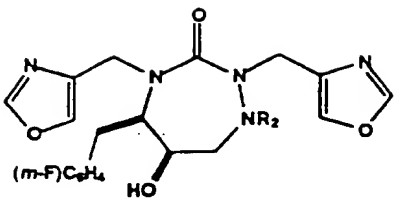

TABLE 51

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

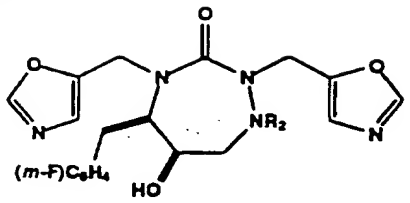

TABLE 52

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

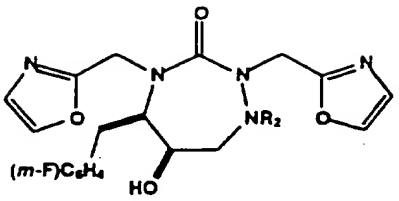

TABLE 53

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

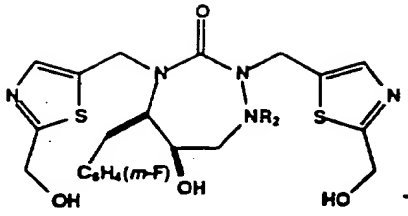

TABLE 54

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

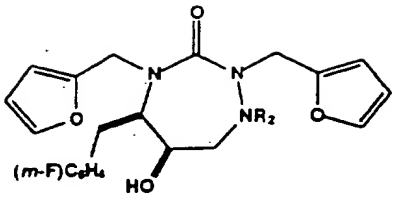

TABLE 55

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

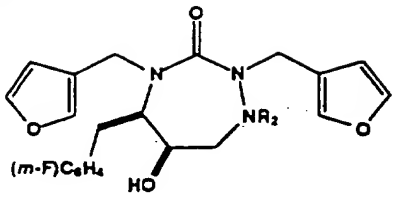

TABLE 56

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

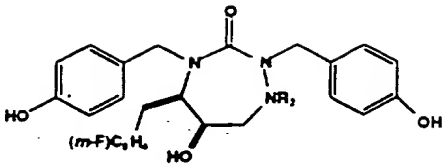

TABLE 57

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

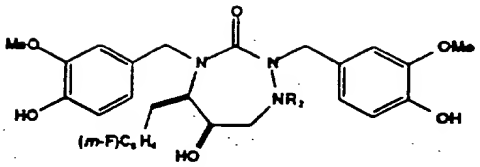

TABLE 58

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

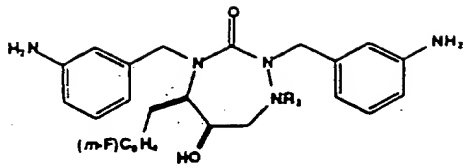

TABLE 59

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

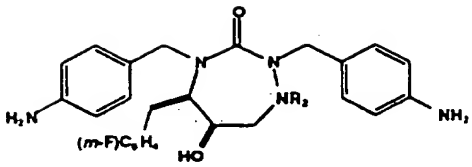

TABLE 60

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

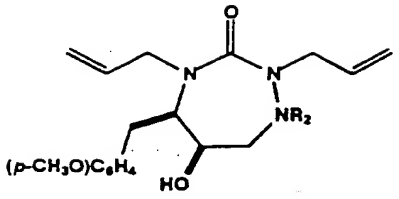

TABLE 61

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

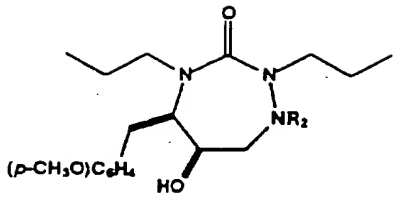

TABLE 62

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

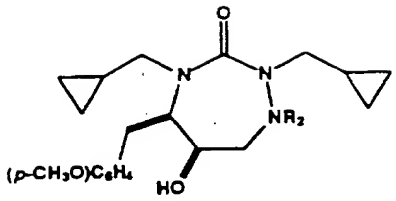

TABLE 63

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

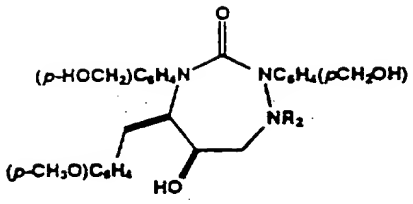

TABLE 64

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

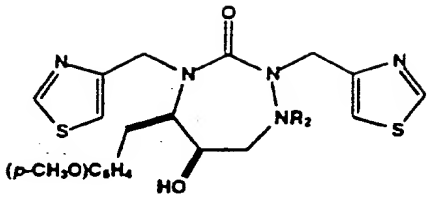

TABLE 65

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

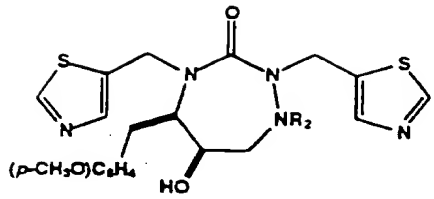

TABLE 66

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

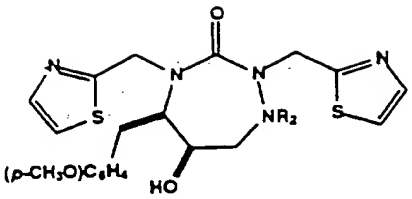

TABLE 67

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

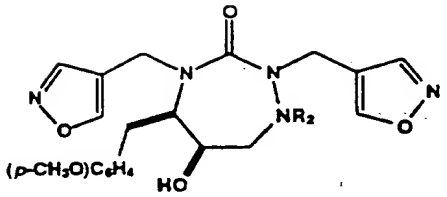

TABLE 68

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

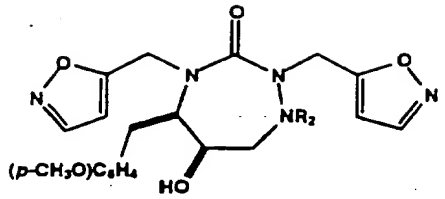

TABLE 69

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

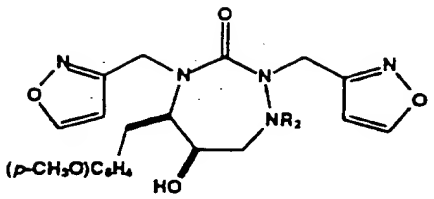

TABLE 70

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

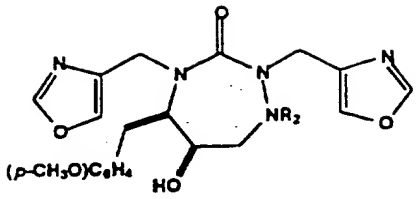

TABLE 71

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

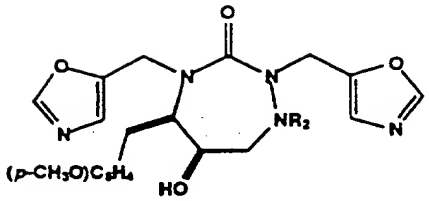

TABLE 72

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

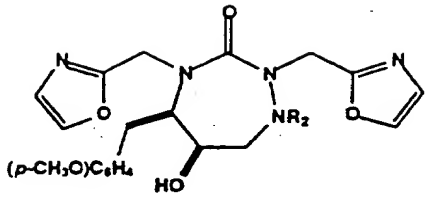

TABLE 73

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

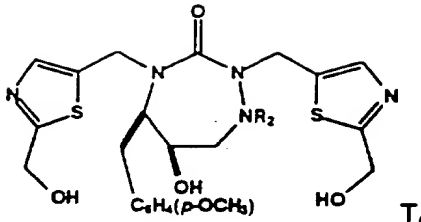

TABLE 74

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

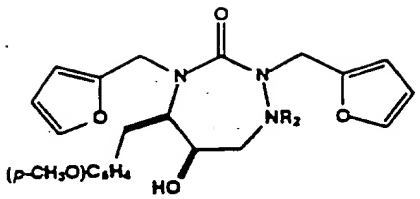

TABLE 75

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

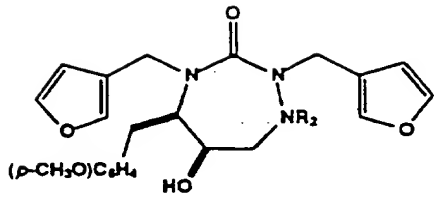

TABLE 76

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

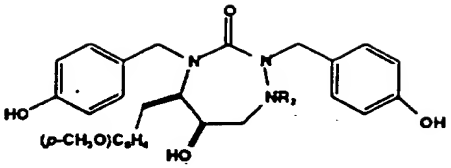

TABLE 77

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

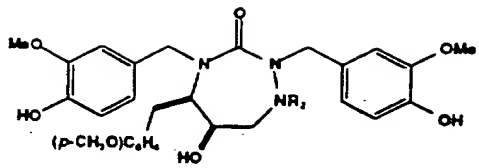

TABLE 78

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

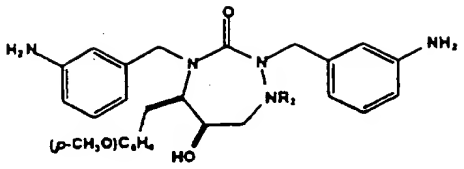

TABLE 79

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

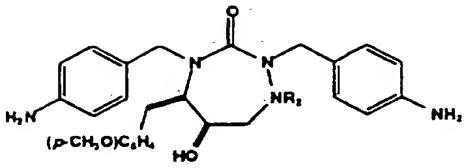

TABLE 80

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

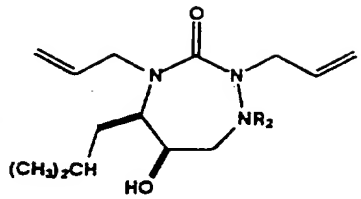

TABLE 81

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

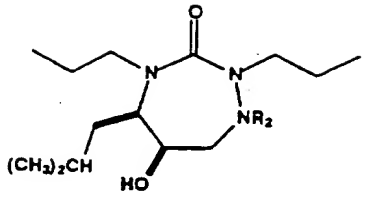

TABLE 82

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

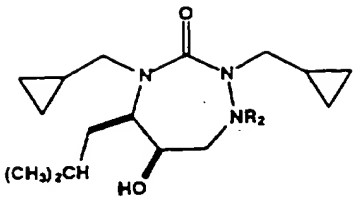

TABLE 83

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

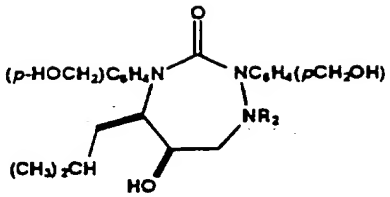

TABLE 84

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

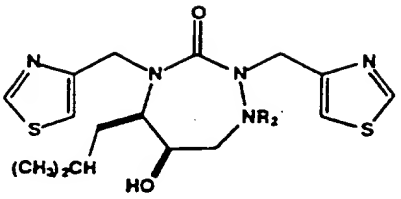

TABLE 85

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

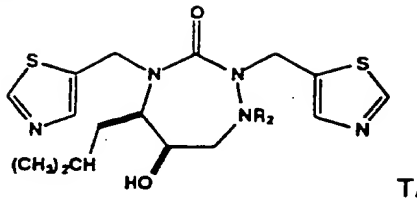

TABLE 86

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

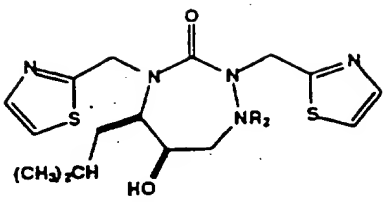

TABLE 87

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

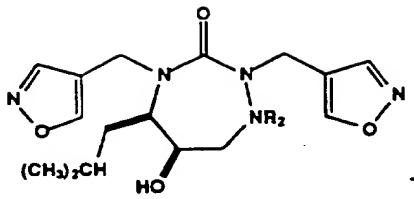

TABLE 88

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

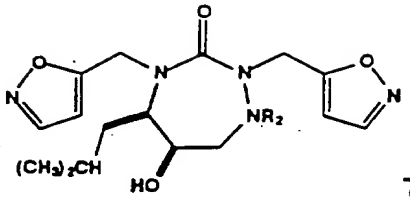

TABLE 89

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

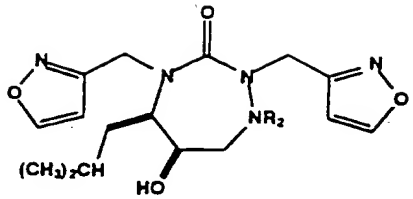

TABLE 90

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

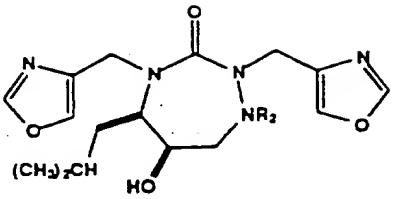

TABLE 91

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

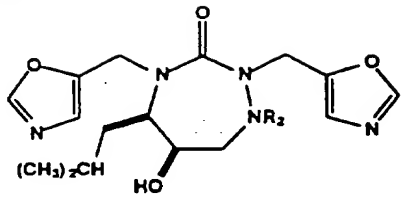

TABLE 92

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

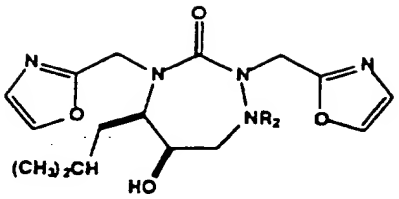

TABLE 93

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

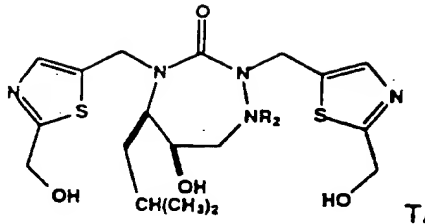

TABLE 94

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

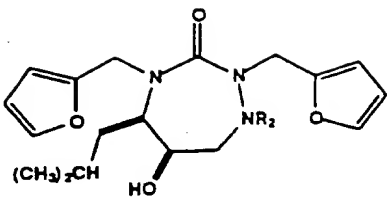

TABLE 95

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

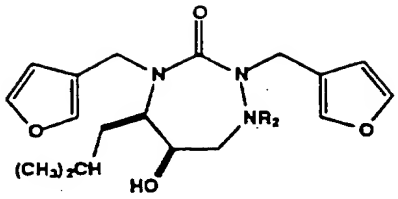

TABLE 96

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

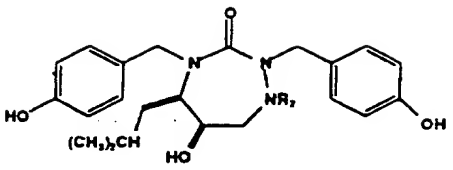

TABLE 97

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

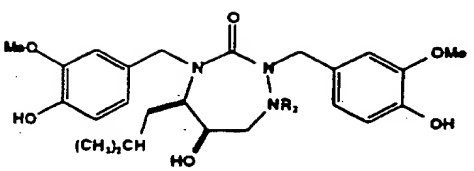

TABLE 98

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

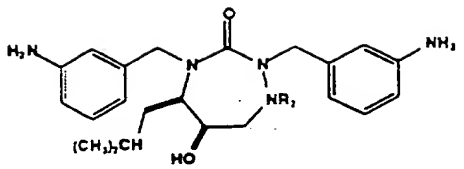

TABLE 99

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

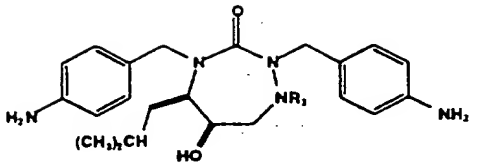

TABLE 100

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

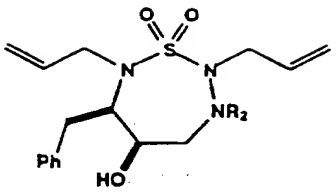

TABLE 101

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

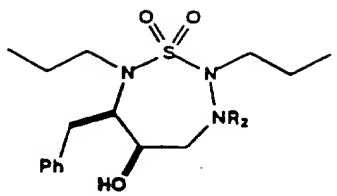

TABLE 102

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

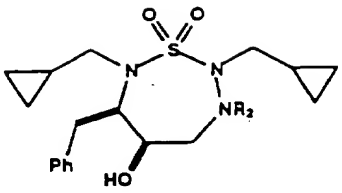

TABLE 103

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

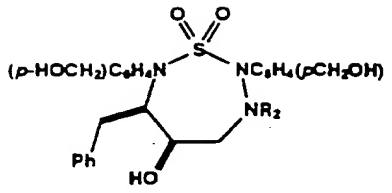

TABLE 104

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

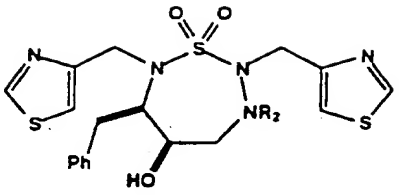

TABLE 105

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

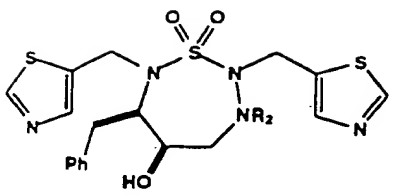

TABLE 106

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

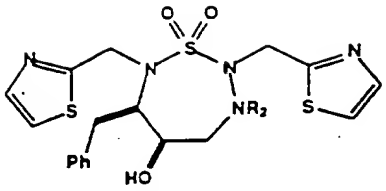

TABLE 107

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

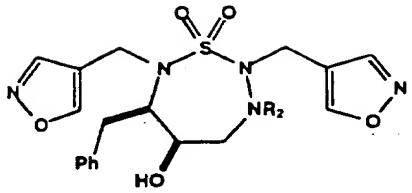

TABLE 108

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

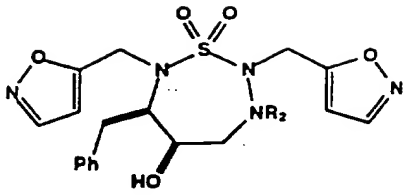

TABLE 109

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

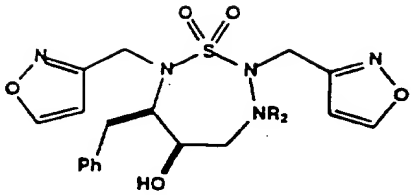

TABLE 110

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

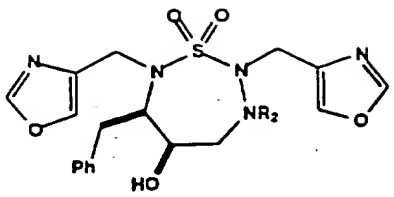

TABLE 111

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

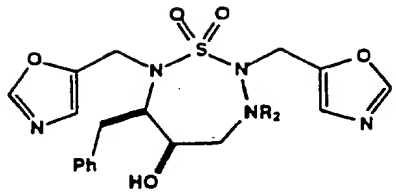

TABLE 112

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

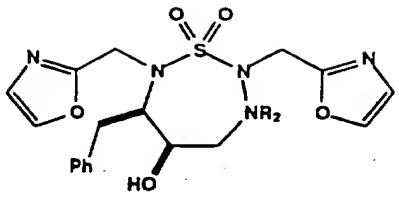

TABLE 113

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

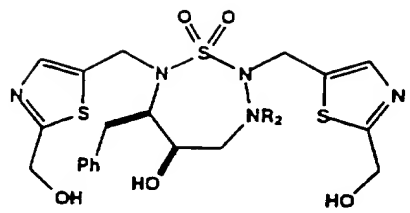

TABLE 114

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

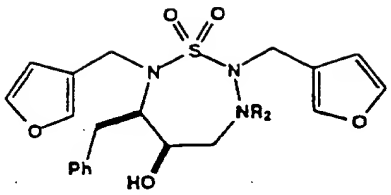

TABLE 115

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

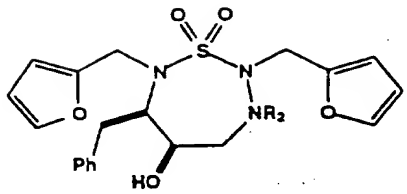

TABLE 116

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

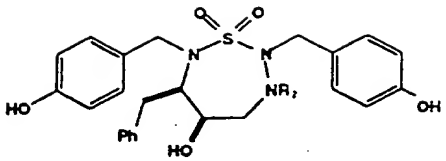

TABLE 117

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

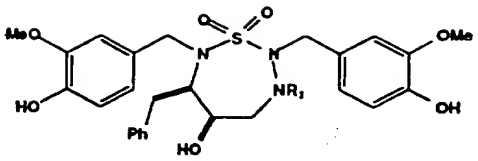

TABLE 118

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

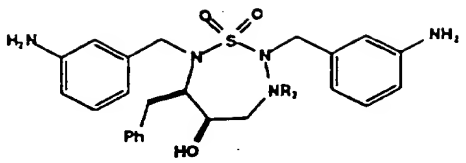

TABLE 119

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

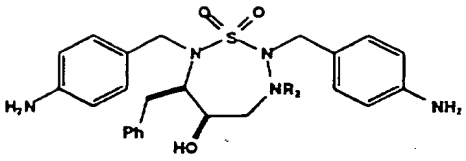

TABLE 120

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

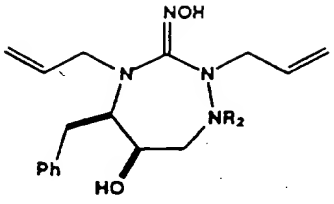

TABLE 121

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

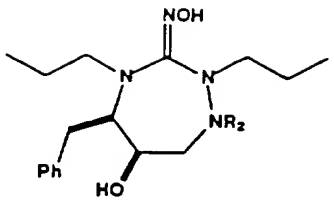

TABLE 122

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

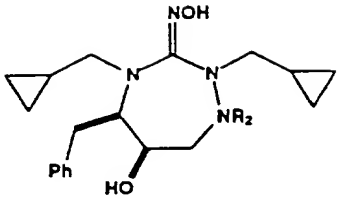

TABLE 123

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

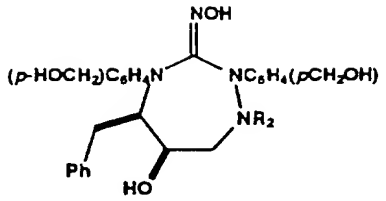

TABLE 124

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

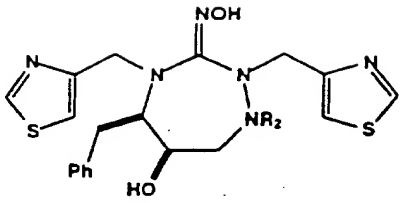

TABLE 125

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

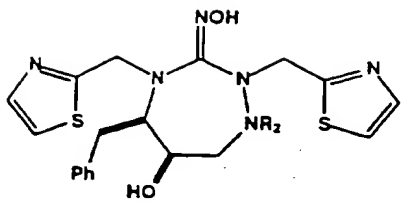

TABLE 126

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

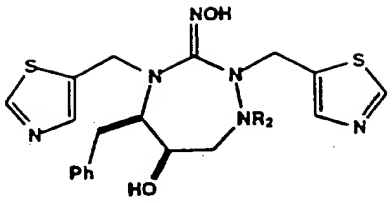

TABLE 127

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

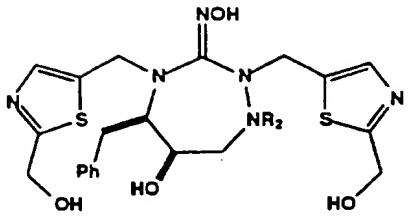

TABLE 128

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

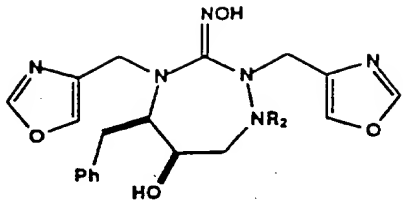

TABLE 129

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

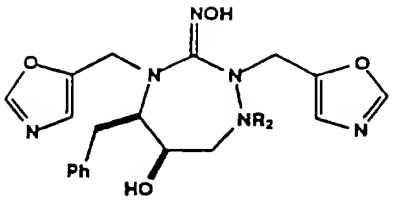

TABLE 130

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

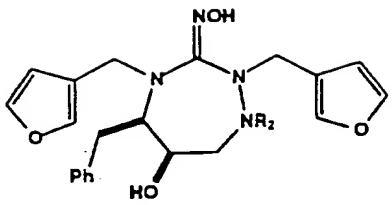

TABLE 131

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

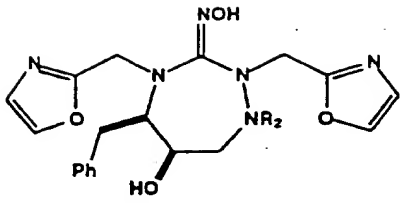

TABLE 132

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

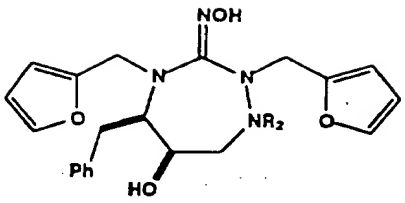

TABLE 133

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

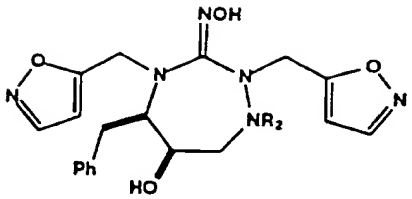

TABLE 134

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

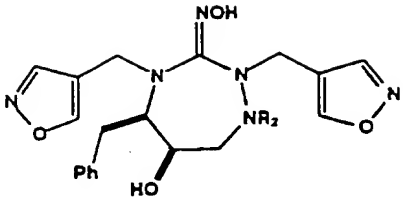

TABLE 135

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

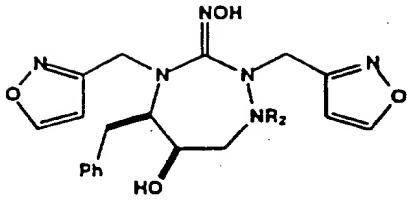

TABLE 136

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

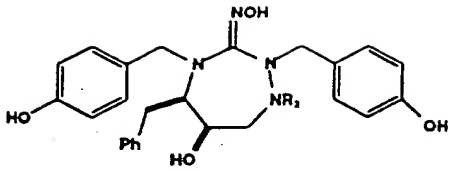

TABLE 137

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

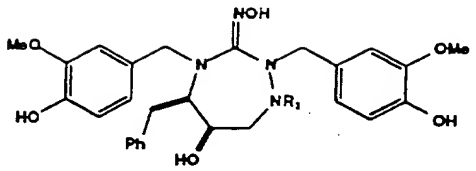

TABLE 138

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

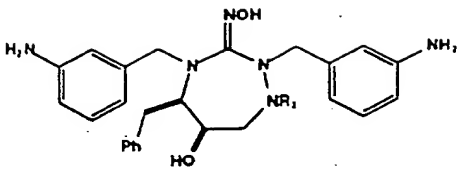

TABLE 139

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

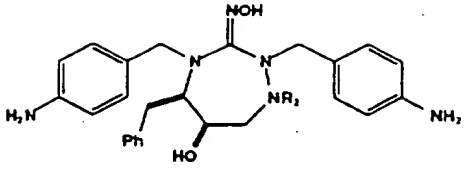

TABLE140

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

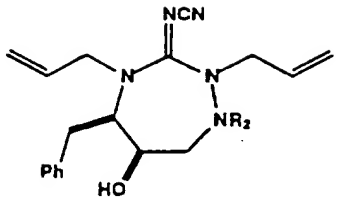

TABLE 141

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

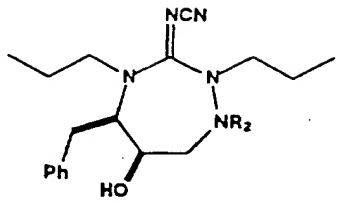

TABLE 142

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

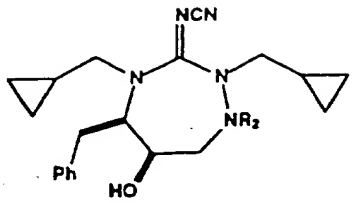

TABLE 143

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

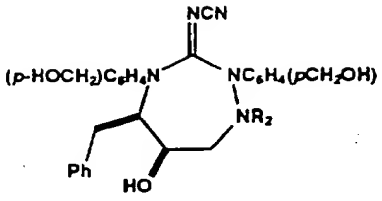

TABLE 144

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

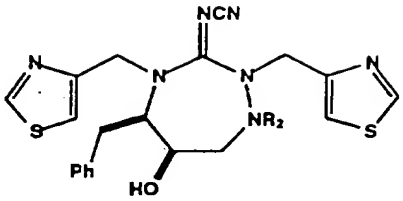

TABLE 145

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

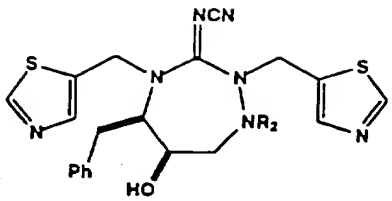

TABLE 146

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

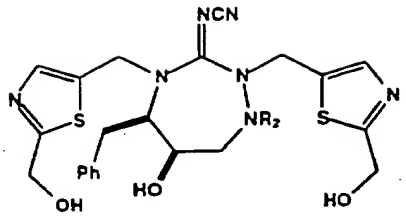

TABLE 147

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

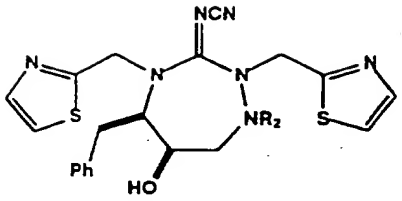

TABLE 148

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

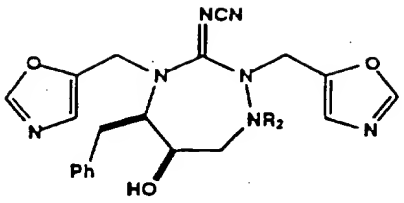

TABLE 149

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

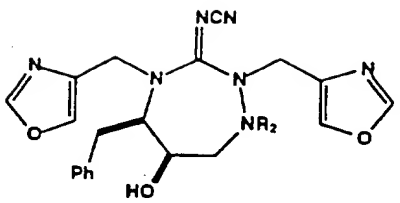

TABLE 150

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

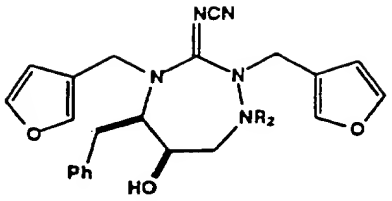

TABLE 151

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

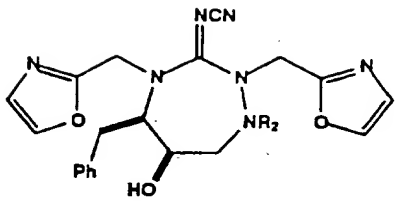

TABLE 152

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

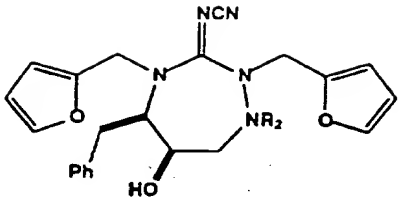

TABLE 153

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

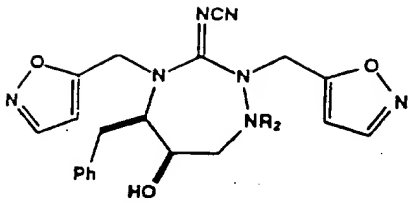

TABLE 154

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

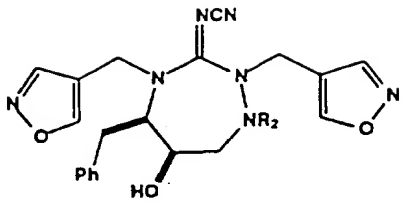

TABLE 155

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

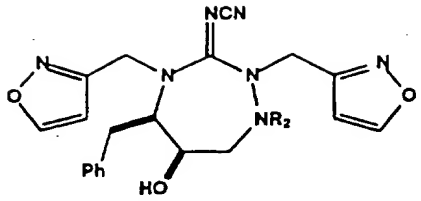

TABLE 156

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

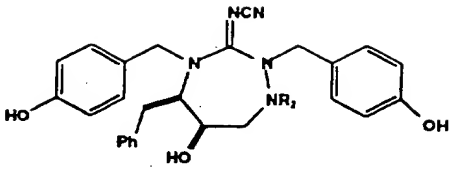

TABLE 157

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

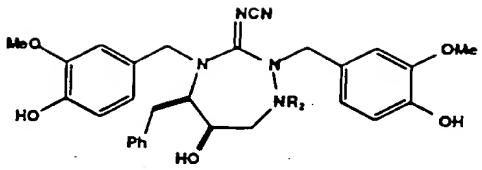

TABLE 158

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
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cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

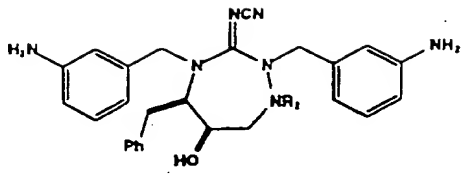

TABLE 159

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
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cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

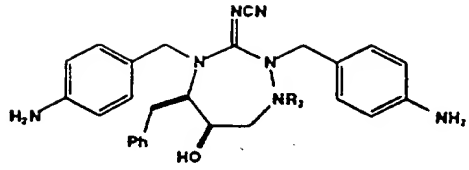


TABLE 160

R_2
benzoyl
acetyl
propionyl
2-methylpropionyl
2,2-dimethylpropionyl
butyryl
3-methylbutyryl
2-ethylbutyryl
valeryl
2-propylvaleryl
cyclopropanoyl
cyclobutanoyl
cyclopentanoyl
cyclohexanoyl
2-hydroxyacetyl
3-hydroxypropionyl
4-hydroxybutyryl
5-hydroxyvaleryl
6-hydroxyhexanoyl
7-hydroxyheptanoyl
N,N-dimethylglycyl
3-(N,N-dimethylamino)propionyl
4-(N,N-dimethylamino)butyryl
5-(N,N-dimethylamino)valeryl
6-(N,N-dimethylamino)hexanoyl
7-(N,N-dimethylamino)heptanoyl
4-morpholinylacetyl
methoxyacetyl
t-butoxycarbonyl
2-furoyl
3-furoyl
methanesulfonyl

Fluorogenic Assay for Screening Inhibitors of HIV Protease

The inhibitory potency of the compounds of the invention can be determined by the following method.

A compound of the invention is dissolved in DMSO and a small aliquot further diluted with DMSO to 100 times the final concentration desired for testing. The reaction is carried out in a 6 X 50 mm tube in a total volume of 300 microliters. The final concentrations of the components in the reaction buffer are: 125 mM sodium acetate, 1 M sodium chloride, 5 mM dithiothreitol, 0.5 mg/ml bovine serum albumin, 1.3 μM fluorogenic substrate, 2% (v/v) dimethylsulfoxide, pH 4.5. After addition of inhibitor, the reaction mixture is placed in the fluorometer cell holder and incubated at 30°C for several minutes. The reaction is initiated by the addition of a small aliquot of cold HIV protease. The fluorescence intensity (excitation 340 nM, emmision 490 nM) is recorded as a function of time. The reaction rate is determined for the first six to eight minutes. The observed rate is directly proportional to the moles of substrate cleaved per unit time. The percent inhibition is 100 X (1 - (rate in presence of inhibitor)/(rate in absence of inhibitor)).

Fluorogenic substrate: Dabcyl-Ser-Gln-Asn-Tyr-Pro-Ile-Val-Gln-EDANS wherein DABCYL = 4-(4-dimethylamino-phenyl)azobenzoic acid and EDANS = 5-((2-aminoethyl)amino)-naphthalene-1-sulfonic acid.

Table I shows the inhibitory potencies of compounds of the invention against HIV-1 protease.

TABLE 1

Compound of Example	Percent Inhibition	Inhibitor Concentration (nanomolar)
2C	50	18
3C	50	13
4C	50	11
5C	50	6.8
8B	50	1.5
9	60	0.5
10	50	0.5
11B	59	0.5
12B	65	0.5
13B	72	0.5
14B	56	1.0
15B	43	0.5
16B	65	0.5
17	50	33
18B	50	3.9
19B	50	1.1
20B	50	13
21D	59	0.5
22D	41	0.5
23D	50	6.6
24	56	0.5
25	66	0.5
26	50	4.9
27	56	1.0

Antiviral Activity

The anti-HIV activity of the compounds of the invention can be determined in MT4 cells according to the procedure of Kempf, et. al. (*Antimicrob. Agents Chemother.* **1991**, *35*, 2209). The IC_{50} is the concentration of compound that gives 50% inhibition of the cytopathic effect of HIV. The LC_{50} is the concentration of compound at which 50% of the cells remain viable.

Table II shows the inhibitory potencies of compounds of the invention against HIV-1_{3B} in MT4 cells.

TABLE II

Compound of Example	IC_{50} (micromolar)	LC_{50} (micromolar)
2C	4.06	>100
3C	2.80	>100
4C	2.90	>100
5C	6.8	63
8B	1.92	17.3
9	0.17	100
10	0.084	52
11B	0.07	26.8
12B	0.030	56.2
13B	0.029	41.4
14B	0.14	19.4
15B	0.33	16.6
16B	0.028	28.0
17	0.83	84.1
18B	1.51	>100
19B	0.37	>100
21D	0.48	>100
22D	0.86	>100

23D	3.0	71.6
24	0.86	>100
25	0.037	59.5
26	5.12	10
27	0.15	77.1

The compounds of the present invention can be used in the form of salts derived from inorganic or organic acids. These salts include but are not limited to the following: acetate, adipate, alginate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, digluconate, cyclopentanepropionate, dodecylsulfate, ethanesulfonate, glucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, fumarate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxy-ethanesulfonate (isethionate), lactate, maleate, methanesulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, pamoate, pectinate, persulfate, 3-phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, p-toluenesulfonate and undecanoate. Also, the basic nitrogen-containing groups can be quaternized with such agents as loweralkyl halides, such as methyl, ethyl, propyl, and butyl chloride, bromides, and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl, and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl bromides, and others. Water or oil-soluble or dispersible products are thereby obtained.

Examples of acids which may be employed to form pharmaceutically acceptable acid addition salts include such inorganic acids as hydrochloric acid, sulphuric acid and phosphoric acid and such organic acids as oxalic acid, maleic acid, succinic acid and citric acid. Other salts include salts with alkali metals or alkaline earth metals, such as sodium, potassium, calcium or magnesium or with organic bases.

The compounds of the present invention can also be used in the form of esters. Examples of such esters include a hydroxyl-substituted compound of formula **A** or **B** which has been acylated with a naturally occurring α-amino acid residue which is optionally N-protected, a phosphate function, a hemisuccinate

residue, an acyl residue of the formula R*C(O)- or R*C(S)- wherein R* is hydrogen, loweralkyl, haloalkyl, alkoxy, thioalkoxy, alkoxyalkyl, thioalkoxyalkyl or haloalkoxy, or an acyl residue of the formula R_a-C(R_b)(R_d)-C(O)- or R_a-C(R_b)(R_d)-C(S)- wherein R_b and R_d are independently selected from hydrogen and loweralkyl and R_a is -N(R_e)(R_f), -OR_e or -SR_e wherein R_e and R_f are independently selected from hydrogen, loweralkyl and haloalkyl, or an amino-acyl residue of the formula $R_{180}NH(CH_2)_2NHCH_2C(O)$- or $R_{180}NH(CH_2)_2OCH_2C(O)$- wherein R_{180} is hydrogen, loweralkyl, arylalkyl, cycloalkylalkyl, alkanoyl, benzoyl or a naturally occurring α-amino acyl group. The amino acid esters of particular interest are those derived from the naturally occurring α-amino acids, however, other amino acid residues can also be used, including those wherein the amino acyl group is -C(O)$CH_2NR_{200}R_{201}$ wherein R_{200} and R_{201} are independently selected from hydrogen and loweralkyl or the group -$NR_{200}R_{201}$ forms a nitrogen containing heterocyclic ring. These esters serve as pro-drugs of the compounds of the present invention and also serve to increase the solubility of these substances in the gastrointestinal tract. These esters also serve to increase solubility for intravenous administration of the compounds. Other prodrugs include a hydroxyl-substituted compound of formula **A** or **B** wherein the hydroxyl group is functionalized with a substituent of the formula -CH(R_g)OC(O)R_{181} or -CH(R_g)OC(S)R_{181} wherein R_{181} is loweralkyl, haloalkyl, alkoxy, thioalkoxy or haloalkoxy and R_g is hydrogen, loweralkyl, haloalkyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl or dialkylaminocarbonyl. Such prodrugs can be prepared according to the procedure of Schreiber (Tetrahedron Lett. **1983**, *24*, 2363) by ozonolysis of the corresponding methallyl ether in methanol followed by treatment with acetic anhydride.

The prodrugs of this invention are metabolized in vivo to provide the hydroxyl-substituted compound of formula **A** or **B**. The preparation of the prodrug esters is carried out by reacting a hydroxyl-substituted compound of formula **A** or **B** with an activated amino acyl, phosphoryl, hemisuccinyl or acyl derivative as defined above. The resulting product is then deprotected to provide the desired pro-drug ester. Prodrugs of the invention can also be prepared by alkylation of the hydroxyl group with (haloalkyl)esters,

transacetalization with bis-(alkanoyl)acetals or condensation of the hydroxyl group with an activated aldehyde followed by acylation of the intermediate hemiacetal.

The compounds of the invention are useful for inhibiting retroviral protease, in particular HIV protease, in vitro or in vivo (especially in mammals and in particular in humans). The compounds of the present invention are also useful for the inhibition of retroviruses in vivo, especially human immunodeficiency virus (HIV). The compounds of the present invention are also useful for the treatment or prophylaxis of diseases caused by retroviruses, especially acquired immune deficiency syndrome or an HIV infection, in a human or other mammal.

Total daily dose administered to a human or other mammal host in single or divided doses may be in amounts, for example, from about 0.001 to about 1000 mg/kg body weight daily and more usually from about 0.1 to about 50 mg/kg body weight daily. Dosage unit compositions may contain such amounts of submultiples thereof to make up the daily dose.

The amount of active ingredient that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated and the particular mode of administration.

It will be understood, however, that the specific dose level for any particular patient will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of administration, route of administration, rate of excretion, drug combination, and the severity of the particular disease undergoing therapy.

The compounds of the present invention may be administered orally, parenterally, sublingually, by inhalation spray, rectally, or topically in dosage unit formulations containing conventional nontoxic pharmaceutically acceptable carriers, adjuvants, and vehicles as desired. Topical administration may also involve the use of transdermal administration such as transdermal patches or iontophoresis devices. The term parenteral as used herein includes subcutaneous injections, intravenous, intramuscular, intrasternal injection, or infusion techniques.

Injectable preparations, for example, sterile injectable aqueous or oleagenous suspensions may be formulated according to the known art using

suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution or suspension in a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-propanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

Suppositories for rectal administration of the drug can be prepared by mixing the drug with a suitable nonirritating excipient such as cocoa butter and polyethylene glycols which are solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum and release the drug.

Solid dosage forms for oral administration may include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound may be admixed with at least one inert diluent such as sucrose lactose or starch. Such dosage forms may also comprise, as is normal practice, additional substances other than inert diluents, e.g., lubricating agents such as magnesium stearate. In the case of capsules, tablets, and pills, the dosage forms may also comprise buffering agents. Tablets and pills can additionally be prepared with enteric coatings.

Liquid dosage forms for oral administration may include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs containing inert diluents commonly used in the art, such as water. Such compositions may also comprise adjuvants, such as wetting agents, emulsifying and suspending agents, and sweetening, flavoring, and perfuming agents.

The compounds of the present invention can also be administered in the form of liposomes. As is known in the art, liposomes are generally derived from phospholipids or other lipid substances. Liposomes are formed by mono- or multi-lamellar hydrated liquid crystals that are dispersed in an aqueous medium. Any non-toxic, physiologically aceptable and metabolizable lipid capabale of forming liposomes can be used. The present compositions in liposome form can contain, in addition to a compound of the present invention,

stabilizers, preservatives, excipients, and the like. The preferred lipids are the phospholipids and phosphatidyl cholines (lecithins), both natural and synthetic.

Methods to form liposomes are known in the art. See, for example, Prescott, Ed., Methods in Cell Biology, Volume XIV, Academic Press, New York, N.Y. (1976), p. 33 et seq.

While the compounds of the invention can be administered as the sole active pharmaceutical agent, they can also be used in combination with one or more immunomodulators, antiviral agents, other antiinfective agents or vaccines. Other antiviral agents to be administered in combination with a compound of the present invention include AL-721, beta interferon, polymannoacetate, reverse transcriptase inhibitors (for example, zalcitabine (ddC), didanosine (ddI), BCH-189, AzdU, carbovir, DDA, D4C, stavudine (d4T), DP-AZT, FLT (fluorothymidine), BCH-189, 5-halo-3'-thia-dideoxycytidine, PMEA, zidovudine (AZT) and the like), non-nucleoside reverse transcriptase inhibitors (for example, R82193, L-697,661, BI-RG-587 (nevirapine), retroviral protease inhibitors (for example, HIV protease inhibitors such as Ro 31-8959, SC-52151, KNI-227, KNI-272 and the like), HEPT compounds, L,697,639, R82150, U-87201E and the like), TAT inhibitors (for example, RO-24-7429 and the like), trisodium phosphonoformate, HPA-23, eflonithine, Peptide T, Reticulose (nucleophosphoprotein), ansamycin LM 427, trimetrexate, UA001, ribavirin, alpha interferon, oxetanocin, oxetanocin-G, cylobut-G, cyclobut-A, ara-M, BW882C87, foscarnet, BW256U87, BW348U87, L-693,989, BV ara-U, CMV triclonal antibodies, FIAC, HOE-602, HPMPC, MSL-109, TI-23, trifluridine, vidarabine, famciclovir, penciclovir, acyclovir, ganciclovir, castanospermine, rCD4/CD4-IgG, CD4-PE40, butyl-DNJ, hypericin, oxamyristic acid, dextran sulfate and pentosan polysulfate. Immunomodulators that can be administered in combination with a compound of the present invention include bropirimine, Ampligen, anti-human alpha interferon antibody, colony stimulting factor, CL246,738, Imreg-1, Imreg-2, diethydithiocarbamate, interleukin-2, alpha-interferon, inosine pranobex, methionine enkephalin, muramyl-tripeptide, TP-5, erythropoietin, naltrexone, tumor necrosis facator, beta interferon, gamma interferon, interleukin-3, interleukin-4, autologous CD8+ infusion, alpha interferon immunoglobulin, IGF-1, anti-Leu-3A, autovaccination, biostimulation, extracorporeal photophoresis, FK-565, FK-506, G-CSF, GM-CSF, hyperthermia,

isopinosine, IVIG, HIVIG, passive immunotherapy and polio vaccine hyperimmunization. Other antiinfective agents that can be administered in combination with a compound of the present invention include pentamidine isethionate. Any of a variety of HIV or AIDS vaccines (for example, gp120 (recombinant), Env 2-3 (gp120), HIVAC-1e (gp120), gp160 (recombinant), VaxSyn HIV-1 (gp160), Immuno-Ag (gp160), HGP-30, HIV-Immunogen, p24 (recombinant), VaxSyn HIV-1 (p24) can be used in combination with a compound of the present invention.

Other agents that can be used in combination with the compounds of this invention are ansamycin LM 427, apurinic acid, ABPP, AI-721, carrisyn, AS-101, avarol, azimexon, colchicine, compound Q, CS-85, N-acetyl cysteine, (2-oxothiazolidine-4-carboxylate), D-penicillamine, diphenylhydantoin, EL-10, erythropoieten, fusidic acid, glucan, HPA-23, human growth hormone, hydroxchloroquine, iscador, L-ofloxacin or other quinolone antibiotics, lentinan, lithium carbonate, MM-1, monolaurin, MTP-PE, naltrexone, neurotropin, ozone, PAI, panax ginseng, pentofylline, pentoxifylline, Peptide T, pine cone extract, polymannoacetate, reticulose, retrogen, ribavirin, ribozymes, RS-47, Sdc-28, silicotungstate, THA, thymic humoral factor, thymopentin, thymosin fraction 5, thymosin alpha one, thymostimulin, UA001, uridine, vitamin B12 and wobemugos.

Other agents that can be used in combination with the compounds of this invention are antifungals such as amphotericin B, clotrimazole, flucytosine, fluconazole, itraconazole, ketoconazole and nystatin and the like.

Other agents that can be used in combination with the compounds of this invention are antibacterials such as amikacin sulfate, azithromycin, ciprofloxacin, tosufloxacin, clarithromycin, clofazimine, ethambutol, isoniazid, pyrazinamide, rifabutin, rifampin, streptomycin and TLC G-65 and the like.

Other agents that can be used in combination with the compounds of this invention are anti-neoplastics such as alpha interferon, COMP (cyclophosphamide, vincristine, methotrexate and prednisone), etoposide, mBACOD (methotrexate, bleomycin, doxorubicin, cyclophosphamide, vincristine and dexamethasone), PRO-MACE/MOPP(prednisone, methotrexate (w/leucovin rescue), doxorubicin, cyclophosphamide, etoposide/mechlorethamine,

vincristine, prednisone and procarbazine), vincristine, vinblastine, angioinhibins, pentosan polysulfate, platelet factor 4 and SP-PG and the like.

Other agents that can be used in combination with the compounds of this invention are drugs for treating neurological disease such as peptide T, ritalin, lithium, elavil, phenytoin, carbamazipine, mexitetine, heparin and cytosine arabinoside and the like.

Other agents that can be used in combination with the compounds of this invention are anti-protozoals such as albendazole, azithromycin, clarithromycin, clindamycin, corticosteroids, dapsone, DIMP, eflornithine, 566C80, fansidar, furazolidone, L,671,329, letrazuril, metronidazole, paromycin, pefloxacin, pentamidine, piritrexim, primaquine, pyrimethamine, somatostatin, spiramycin, sulfadiazine, trimethoprim, TMP/SMX, trimetrexate and WR 6026 and the like.

Among the preferred agents for treatment of HIV or AIDS in combination with the compounds of this invention are reverse transcriptase inhibitors.

It will be understood that agents which can be combined with the compounds of the present invention for the treatment or prophylaxis of AIDS or an HIV infection are not limited to those listed above, but include in principle any agents useful for the treatment or prophylaxis of AIDS or an HIV infection.

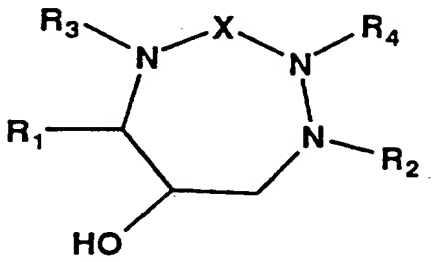
When administered as a combination, the therapeutic agents can be formulated as separate compositions which are given at the same time or different times, or the therapeutic agents can be given as a single composition.

The foregoing is merely illustrative of the invention and is not intended to limit the invention to the disclosed compounds. Variations and changes which are obvious to one skilled in the art are intended to be within the scope and nature of the invention which are defined in the appended claims.

CLAIMS

What is claimed is:

1. A compound of the formula:



wherein R_1 is selected from:

(i) hydrogen,
(ii) loweralkyl,
(iii) aryl,
(iv) thioalkoxyalkyl,
(v) (aryl)alkyl,
(vi) cycloalkyl,
(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,
(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,
(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,
(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,

(xx) loweralkenyl,
(xxi) heterocyclic,
(xxii) (heterocyclic)alkyl),
(xxiii) arylthioalkyl,
(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,
(xxvii) (heterocyclic)oxyalkyl,
(xxviii) arylalkoxyalkyl,
(xxix) arylthioalkoxyalkyl,
(xxx) arylalkylsulfonylalkyl,
(xxxi) (heterocyclic)alkoxyalkyl,
(xxxii) (heterocyclic)thioalkoxyalkyl,
(xxxiii) (heterocyclic)alkylsulfonylalkyl,
(xxxiv) cycloalkyloxyalkyl,
(xxxv) cycloalkylthioalkyl,
(xxxvi) cycloalkylsulfonylalkyl,
(xxxvii) cycloalkylalkoxyalkyl,
(xxxviii) cycloalkylthioalkoxyalkyl,
(xxxix) cycloalkylalkylsulfonylalkyl,
(xl) aminocarbonyl,
(xli) alkylaminocarbonyl,
(xlii) dialkylaminocarbonyl,
(xliii) aroylalkyl,
(xliv) (heterocyclic)carbonylalkyl,
(xlv) polyhydroxyalkyl,
(xlvi) aminocarbonylalkyl,
(xlvii) alkylaminocarbonylalkyl,
(xlviii) dialkylaminocarbonylalkyl,
(xlix) aryloxyalkyl,
(l) alkylsulfonylalkyl and
(li) arylalkoxycarbonylalkyl;

R_2 is R_{2a}-C(O)- or R_{2a}-$S(O)_2$- wherein R_{2a} is selected from:

(i) loweralkyl,
(ii) loweralkenyl,
(iii) cycloalkyl,
(iv) cycloalkenyl,
(v) cycloalkylalkyl,
(vi) cycloalkenylalkyl,
(vii) hydroxyalkyl,
(viii) alkoxyalkyl,
(ix) aminoalkyl,
(x) alkylaminoalkyl,
(xi) dialkylaminoalkyl,
(xii) aryl,
(xiii) arylalkyl,
(xiv) heterocyclic,
(xv) (heterocyclic)alkyl and
(xvi) alkoxy;

R_3 and R_4 are independently selected from:

(i) hydrogen,
(ii) loweralkyl,
(iii) aryl,
(iv) thioalkoxyalkyl,
(v) (aryl)alkyl,
(vi) cycloalkyl,
(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,
(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,

(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,
(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,
(xx) loweralkenyl,
(xxi) heterocyclic,
(xxii) (heterocyclic)alkyl),
(xxiii) arylthioalkyl,
(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,
(xxvii) (heterocyclic)oxyalkyl,
(xxviii) arylalkoxyalkyl,
(xxix) arylthioalkoxyalkyl,
(xxx) arylalkylsulfonylalkyl,
(xxxi) (heterocyclic)alkoxyalkyl,
(xxxii) (heterocyclic)thioalkoxyalkyl,
(xxxiii) (heterocyclic)alkylsulfonylalkyl,
(xxxiv) cycloalkyloxyalkyl,
(xxxv) cycloalkylthioalkyl,
(xxxvi) cycloalkylsulfonylalkyl,
(xxxvii) cycloalkylalkoxyalkyl,
(xxxviii) cycloalkylthioalkoxyalkyl,
(xxxix) cycloalkylalkylsulfonylalkyl,
(xl) aroylalkyl,
(xli) (heterocyclic)carbonylalkyl,
(xlii) polyhydroxyalkyl,
(xliii) aminocarbonylalkyl,
(xliv) alkylaminocarbonylalkyl,
(xlv) dialkylaminocarbonylalkyl,
(xlv) aryloxyalkyl,
(xlvi) alkylsulfonylalkyl,
(xlvii) carboxyalkoxyalkyl,
(xlviii) (alkoxycarbonyl)alkoxyalkyl,

(xlix) (amino)carboxyalkyl,
(l) ((N-protected)amino)carboxyalkyl,
(li) (alkylamino)carboxyalkyl,
(lii) ((N-protected)alkylamino)carboxyalkyl,
(liii) (dialkylamino)carboxyalkyl,
(liv) (amino)alkoxycarbonylalkyl,
(lv) ((N-protected)amino)alkoxycarbonylalkyl,
(lvi) (alkylamino)alkoxycarbonylalkyl,
(lvii) ((N-protected)alkylamino)alkoxycarbonylalkyl,
(lviii) (dialkylamino)alkoxycarbonylalkyl,
(lix) (polyalkoxy)alkyl,
(lx) (hydroxyamino)alkyl,
(lxi) (alkoxyamino)alkyl,
(lxii) dihydroxyalkyl,
(lxiii) (alkoxy)(alkyl)aminoalkyl and
(lxiv) arylalkoxycarbonylalkyl; and

X is

(i) -C(=Y)- wherein Y is O, S or N(R_5) wherein R_5 is loweralkyl, hydroxy, amino, alkylamino, dialkylamino, alkoxy, benzyloxy, cyano or nitro;
(ii) -S(O)- or
(iii) -$S(O)_2$-;

or a pharmaceutically acceptable salt, ester or prodrug thereof.

2. The compound of Claim 1 wherein R_1 is loweralkyl or arylalkyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is loweralkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, aryl or arylalkyl; R_3 and R_4 are independently selected from loweralkyl, loweralkenyl, cycloalkylalkyl, arylalkyl or (heterocyclic)alkyl; and X is -C(=O)-, -C(=N-OH)-, -C(=N-CN)- or -$S(O)_2$-.

3. The compound of Claim 1 wherein R_1 is loweralkyl, benzyl, alkoxy-substituted benzyl or halo-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is loweralkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, aryl or arylalkyl; R_3 and R_4 are independently selected from loweralkyl, loweralkenyl, cycloalkylalkyl, benzyl, hydroxy-substituted benzyl, hydroxyalkyl-substituted benzyl, alkoxy-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substitutents are hydroxy and alkoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)-, -C(=N-OH)-, -C(=N-CN)- or $-S(O)_2-$.

4. The compound of Claim 1 wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is CH_3-, CH_3-$(CH_2)_2$-, $(CH_3)_2CHCH_2$-, $CH_3(CH_2)_3$-, $(CH_3(CH_2)_2)_2CH$-, cyclopentyl, $HOCH_2(CH_2)_3$-, $HOCH_2(CH_2)_2$- or $HOCH_2$-; R_3 and R_4 are independently selected from loweralkyl, allyl, cyclopropylmethyl, benzyl, hydroxy-substituted benzyl, methoxy-substituted benzyl, hydroxymethyl-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substituents are hydroxy and methoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)- or $-S(O)_2-$.

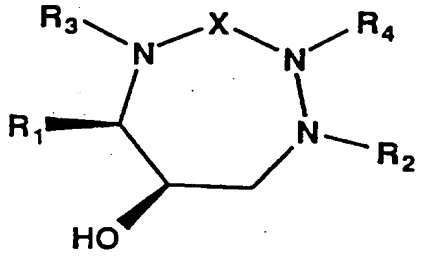
5. The compound of Claim 1 wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is CH_3-, CH_3-$(CH_2)_2$-, $(CH_3)_2CHCH_2$-, $CH_3(CH_2)_3$-, $(CH_3(CH_2)_2)_2CH$-, cyclopentyl, $HOCH_2(CH_2)_3$-, $HOCH_2(CH_2)_2$- or $HOCH_2$-; R_3 and R_4 are independently selected from loweralkyl, allyl, cyclopropylmethyl, benzyl, hydroxy-substituted benzyl, methoxy-substituted benzyl, hydroxymethyl-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substituents are hydroxy and methoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)-.

6. The compound of Claim 1 wherein R_1 is benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is CH_3-, CH_3-

$(CH_2)_2$-, $(CH_3)_2CHCH_2$-, $CH_3(CH_2)_3$-, $(CH_3(CH_2)_2)_2CH$-, cyclopentyl, $HOCH_2(CH_2)_3$-, $HOCH_2(CH_2)_2$- or $HOCH_2$-; R_3 and R_4 are independently selected from loweralkyl, allyl, cyclopropylmethyl, benzyl, hydroxy-substituted benzyl, methoxy-substituted benzyl, hydroxymethyl-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substituents are hydroxy and methoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)-.

7. The compound of Claim 1 wherein R_1 is benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is $(CH_3)_2CHCH_2$-; R_3 and R_4 are independently selected from 4-hydroxybenzyl, 4-aminobenzyl and 3-aminobenzyl; and X is -C(=O)-.

8. The compound according to Claim 1 of the formula:



wherein R_1, R_2, R_3, R_4 and X are as defined therein.

9. The compound of Claim 8 wherein R_1 is loweralkyl or arylalkyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is loweralkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, aryl or arylalkyl; R_3 and R_4 are independently selected from loweralkyl, loweralkenyl, cycloalkylalkyl, arylalkyl or (heterocyclic)alkyl; and X is -C(=O)-, -C(=N-OH)-, -C(=N-CN)- or $-S(O)_2$-.

10. The compound of Claim 8 wherein R_1 is loweralkyl, benzyl, alkoxy-substituted benzyl or halo-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is loweralkyl, cycloalkyl, cycloalkylalkyl, hydroxyalkyl, aryl or arylalkyl; R_3 and R_4 are independently selected from loweralkyl, loweralkenyl, cycloalkylalkyl, benzyl, hydroxy-substituted benzyl, hydroxyalkyl-substituted benzyl, alkoxy-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the

substitutents are hydroxy and alkoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)-, -C(=N-OH)-, -C(=N-CN)- or $-S(O)_2-$.

11. The compound of Claim 8 wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is CH_3-, $CH_3-(CH_2)_2-$, $(CH_3)_2CHCH_2-$, $CH_3(CH_2)_3-$, $(CH_3(CH_2)_2)_2CH-$, cyclopentyl, $HOCH_2(CH_2)_3-$, $HOCH_2(CH_2)_2-$ or $HOCH_2-$; R_3 and R_4 are independently selected from loweralkyl, allyl, cyclopropylmethyl, benzyl, hydroxy-substituted benzyl, methoxy-substituted benzyl, hydroxymethyl-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substituents are hydroxy and methoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)- or $-S(O)_2-$.

12. The compound of Claim 8 wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is CH_3-, $CH_3-(CH_2)_2-$, $(CH_3)_2CHCH_2-$, $CH_3(CH_2)_3-$, $(CH_3(CH_2)_2)_2CH-$, cyclopentyl, $HOCH_2(CH_2)_3-$, $HOCH_2(CH_2)_2-$ or $HOCH_2-$; R_3 and R_4 are independently selected from loweralkyl, allyl, cyclopropylmethyl, benzyl, hydroxy-substituted benzyl, methoxy-substituted benzyl, hydroxymethyl-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substituents are hydroxy and methoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)-.

13. The compound of Claim 8 wherein R_1 is benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is CH_3-, $CH_3-(CH_2)_2-$, $(CH_3)_2CHCH_2-$, $CH_3(CH_2)_3-$, $(CH_3(CH_2)_2)_2CH-$, cyclopentyl, $HOCH_2(CH_2)_3-$, $HOCH_2(CH_2)_2-$ or $HOCH_2-$; R_3 and R_4 are independently selected from loweralkyl, allyl, cyclopropylmethyl, benzyl, hydroxy-substituted benzyl, methoxy-substituted benzyl, hydroxymethyl-substituted benzyl, amino-substituted benzyl, disubstituted benzyl wherein the substituents are hydroxy

and methoxy or (heterocyclic)methyl wherein the heterocyclic is thiazolyl, oxazolyl, isoxazolyl or furanyl; and X is -C(=O)-.

14. The compound of Claim 8 wherein R_1 is benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_2 is R_{2a}-C(O)- wherein R_{2a} is $(CH_3)_2CHCH_2$-; R_3 and R_4 are independently selected from 4-hydroxybenzyl, 4-aminobenzyl and 3-aminobenzyl; and X is -C(=O)-.

15. A compound selected from the group consisting of:
(5R,6R)-2,4-Bis-(4-hydroxybenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane;
(5R,6R)-2,4-Bis-(3-aminobenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane; and
(5R,6R)-2,4-Bis-(4-aminobenzyl)-1-(3-methylbutyryl)-5-benzyl-6-hydroxy-3-oxo-1,2,4-triazacycloheptane;
or a pharmaceutically acceptable salt, ester or prodrug thereof.

16. A method for inhibiting HIV protease comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 1.

17. A method for inhibiting HIV protease comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 8.

18. A method for inhibiting HIV protease comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 15.

19. A method for inhibiting HIV comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 1.

20. A method for inhibiting HIV comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 8.

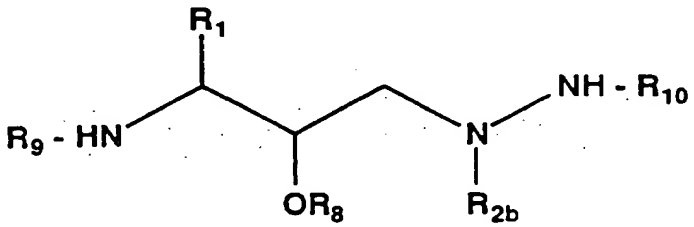
21. A method for inhibiting HIV comprising administering to a human in need thereof a therapeutically effective amount of a compound of Claim 15.

22. A pharmaceutical composition for inhibiting HIV protease comprising a pharmaceutical carrier and a therapeutically effective amount of a compound of Claim 1.

23. A pharmaceutical composition for inhibiting HIV protease comprising a pharmaceutical carrier and a therapeutically effective amount of a compound of Claim 8.

24. A pharmaceutical composition for inhibiting HIV protease comprising a pharmaceutical carrier and a therapeutically effective amount of a compound of Claim 15.

25. A compound of the formula:



wherein R_1 is selected from:

(i) hydrogen,
(ii) loweralkyl,
(iii) aryl,
(iv) thioalkoxyalkyl,

(v) (aryl)alkyl,
(vi) cycloalkyl,
(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,
(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,
(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,
(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,
(xx) loweralkenyl,
(xxi) heterocyclic,
(xxii) (heterocyclic)alkyl),
(xxiii) arylthioalkyl,
(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,
(xxvii) (heterocyclic)oxyalkyl,
(xxviii) arylalkoxyalkyl,
(xxix) arylthioalkoxyalkyl,
(xxx) arylalkylsulfonylalkyl,
(xxxi) (heterocyclic)alkoxyalkyl,
(xxxii) (heterocyclic)thioalkoxyalkyl,
(xxxiii) (heterocyclic)alkylsulfonylalkyl,
(xxxiv) cycloalkyloxyalkyl,
(xxxv) cycloalkylthioalkyl,
(xxxvi) cycloalkylsulfonylalkyl,
(xxxvii) cycloalkylalkoxyalkyl,
(xxxviii) cycloalkylthioalkoxyalkyl,

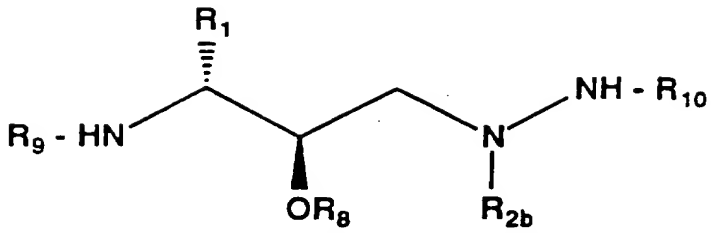
(xxxix) cycloalkylalkylsulfonylalkyl,
(xl) aminocarbonyl,
(xli) alkylaminocarbonyl,
(xlii) dialkylaminocarbonyl,
(xliii) aroylalkyl,
(xliv) (heterocyclic)carbonylalkyl,
(xlv) polyhydroxyalkyl,
(xlvi) aminocarbonylalkyl,
(xlvii) alkylaminocarbonylalkyl,
(xlviii) dialkylaminocarbonylalkyl,
(xlix) aryloxyalkyl,
(l) alkylsulfonylalkyl and
(li) arylalkoxycarbonylalkyl;

R_{2b} is selected from:

(i) hydrogen,
(ii) benzyl,
(iii) nitrobenzyl,
(iv) dimethoxybenzyl,
(v) diphenylmethyl,
(vi) di-(methoxyphenyl)methyl and
(vii) triphenylmethyl;

R_8 is hydrogen or an O-protecting group; and
R_9 and R_{10} are independently selected from hydrogen and an N-protecting group; or an acid addition salt thereof.

26. The compound according to Claim 25 of the formula:



wherein R_1, R_2, R_8, R_9 and R_{10} are as defined therein.

27. The compound of Claim 24 wherein R_1 is loweralkyl or arylalkyl and R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

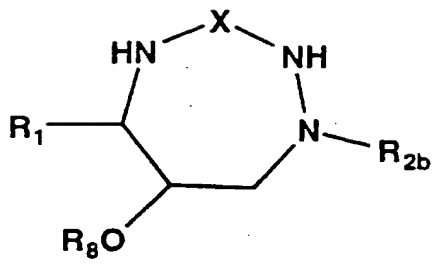
28. The compound of Claim 24 wherein R_1 is loweralkyl, benzyl, alkoxy-substituted benzyl or halo-substituted benzyl; R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

29. The compound of Claim 24 wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

30. The compound of Claim 24 wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; and R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

31. The compound of Claim 24 wherein R_1 is benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl; and R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl.

32. The compound of the formula:



wherein R_1 is selected from:

(i) hydrogen,
(ii) loweralkyl,
(iii) aryl,
(iv) thioalkoxyalkyl,
(v) (aryl)alkyl,
(vi) cycloalkyl,
(vii) cycloalkylalkyl,
(viii) hydroxyalkyl,
(ix) alkoxyalkyl,
(x) aryloxyalkyl,
(xi) haloalkyl,
(xii) carboxyalkyl,
(xiii) alkoxycarbonylalkyl,
(xiv) aminoalkyl,
(xv) (N-protected)aminoalkyl,
(xvi) alkylaminoalkyl,
(xvii) ((N-protected)(alkyl)amino)alkyl,
(xviii) dialkylaminoalkyl,
(xix) guanidinoalkyl,
(xx) loweralkenyl,
(xxi) heterocyclic,
(xxii) (heterocyclic)alkyl),
(xxiii) arylthioalkyl,
(xxiv) arylsulfonylalkyl,
(xxv) (heterocyclic)thioalkyl,
(xxvi) (heterocyclic)sulfonylalkyl,

(xxvii)	(heterocyclic)oxyalkyl,
(xxviii)	arylalkoxyalkyl,
(xxix)	arylthioalkoxyalkyl,
(xxx)	arylalkylsulfonylalkyl,
(xxxi)	(heterocyclic)alkoxyalkyl,
(xxxii)	(heterocyclic)thioalkoxyalkyl,
(xxxiii)	(heterocyclic)alkylsulfonylalkyl,
(xxxiv)	cycloalkyloxyalkyl,
(xxxv)	cycloalkylthioalkyl,
(xxxvi)	cycloalkylsulfonylalkyl,
(xxxvii)	cycloalkylalkoxyalkyl,
(xxxviii)	cycloalkylthioalkoxyalkyl,
(xxxix)	cycloalkylalkylsulfonylalkyl,
(xl)	aminocarbonyl,
(xli)	alkylaminocarbonyl,
(xlii)	dialkylaminocarbonyl,
(xliii)	aroylalkyl,
(xliv)	(heterocyclic)carbonylalkyl,
(xlv)	polyhydroxyalkyl,
(xlvi)	aminocarbonylalkyl,
(xlvii)	alkylaminocarbonylalkyl,
(xlviii)	dialkylaminocarbonylalkyl,
(xlix)	aryloxyalkyl,
(l)	alkylsulfonylalkyl and
(li)	arylalkoxycarbonylalkyl;

R_{2b} is benzyl, nitrobenzyl, dimethoxybenzyl, diphenylmethyl, di-(methoxyphenyl)methyl or triphenylmethyl;

R_8 is hydrogen or an O-protecting group; and

X is

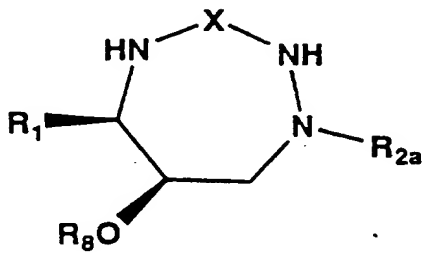
(i) -C(=Y)- wherein Y is O, S or N(R_5) wherein R_5 is loweralkyl, hydroxy, amino, alkylamino, dialkylamino, alkoxy, benzyloxy, cyano or nitro;

(ii) -S(O)- or

(iii) -$S(O)_2$-;

or a salt thereof.

33. The compound according to Claim 32 of the formula:



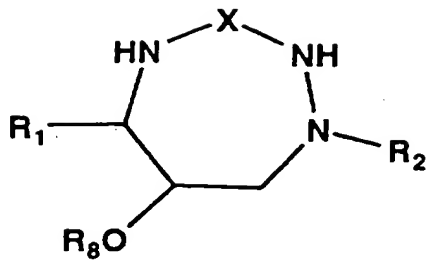
wherein R_1, R_{2a}, R_8 and X are as defined therein.

34. The compound of Claim 32 wherein R_1 is loweralkyl or arylalkyl; R_2 is benzyl and R_8 is an O-protecting group.

35. The compound of Claim 32 wherein R_1 is loweralkyl, benzyl, alkoxy-substituted benzyl or halo-substituted benzyl and X is -C(=O)-.

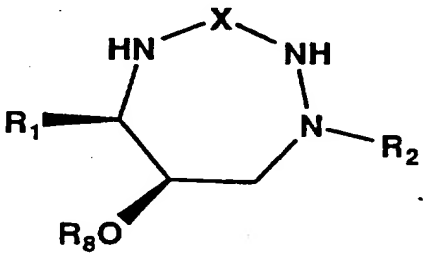
36. The compound of Claim 32 wherein R_1 is isobutyl, benzyl, methoxy-substituted benzyl or fluoro-substituted benzyl and X is -C(=O)-.

37. A process for the preparation of a compound of Claim 1 comprising reacting a compound of the formula:



wherein R_1, R_2, R_8 and X are as defined therein with R_4-Z" wherein Z" is a leaving group and R_4 is as defined therein, followed by reaction of the resulting product with R_3-Z' wherein Z' is a leaving group and R_3 is as defined therein.

38. A process for the preparation of a compound of Claim 8 comprising reacting a compound of the formula:



wherein R_1, R_2, R_8 and X are as defined there with R_4-Z" wherein Z" is a leaving group and R_4 is as defined therein, followed by reaction of the resulting product with R_3-Z' wherein Z' is a leaving group and R_3 is as defined therein.

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 95/09472

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D255/02 A61K31/55 C07D295/08 C07D417/06 C07D403/06
C07D405/06 C07D413/06 C07D417/14 C07C281/02 C07F7/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D C07C C07F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP,A,0 521 827 (CIBA-GEIGY AG) 7 January 1993 see page 94; claim 1 see page 99; claim 11 see page 3, line 1 - page 4, line 17	25-31
A		1-24, 32-38

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

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Date of the actual completion of the international search	Date of mailing of the international search report
20 November 1995	- 4. 12. 95
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Authorized officer Paisdor, B

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JOURNAL OF THE CHEMICAL SOCIETY, CHEMICAL COMMUNICATIONS., no. 13, 7 July 1993 LETCHWORTH GB, pages 1052-1053, H.L. SHAM ET AL. 'Facile Synthesis of Potent HIV-1 Protease Inhibitors containing a Novel Pseudo-symmetric Pipeptide Isostere' see the whole document and in particular formulae 10a-e, and 11	25-31
A		1-24, 32-38
X	WO,A,93 18006 (NARHEX LIMITED) 16 September 1993 see claims 1,5,9-16; examples	25-31
A		1-24, 31-38
X	EP,A,0 604 368 (CIBA-GEIGY AG) 29 June 1994 see abstract; claims; examples	25-31
A		1-24, 32-38
A	WO,A,94 08977 (THE DU PONT MERCK PHARMACEUTICAL COMPANY) 28 April 1994 see page 1, line 5 - page 5, line 12; claims 1,8,10-31	1-38
A	WO,A,92 09297 (SMITHKLINE BEECHAM CORPORATION) 11 June 1992 see page 23; claims	1-38
P,X	WO,A,94 19332 (ABBOTT LABORATORIES) 1 September 1994 see abstract; claims; examples	25-31
A		1-24, 32-38
P,X	WO,A,95 02582 (CIBA-GEIGY AG) 26 January 1995 see the whole document	1-38

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INTERNATIONAL SEARCH REPORT

In ..national application No.
PCT/US95/09472

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 16-21 are directed to a method of treatment of (diagnostic method practised on) the human/animal body, the search has been carried out and based on the alledged effects of the compound/composition.

2. ☒ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

nformation on patent family members

Inte nal Application No
PCT/US 95/09472

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A-0521827	07-01-93	AU-B-	660469	29-06-95
		AU-A-	1937392	07-01-93
		CN-A-	1068333	27-01-93
		JP-A-	5201945	10-08-93
		NZ-A-	243410	24-02-95
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		JP-T-	7504654	25-05-95
EP-A-604368	29-06-94	AU-B-	5247993	07-07-94
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		FI-A-	935753	24-06-94
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		JP-A-	6279386	04-10-94
		NO-A-	934774	24-06-94
		PL-A-	301611	27-06-94
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WO-A-9209297	11-06-92	AU-B-	9122391	25-06-92
		EP-A-	0559793	15-09-93
		JP-T-	6503568	21-04-94
		US-A-	5438118	01-08-95
WO-A-9419332	01-09-94	US-A-	5461067	24-10-95
		CA-A-	2155338	01-09-94
WO-A-9502582	26-01-95	AU-B-	7491694	13-02-95